

FIG. 1

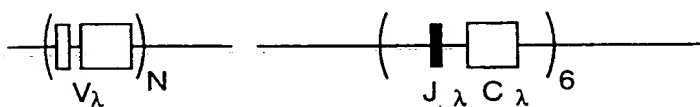


FIG. 2

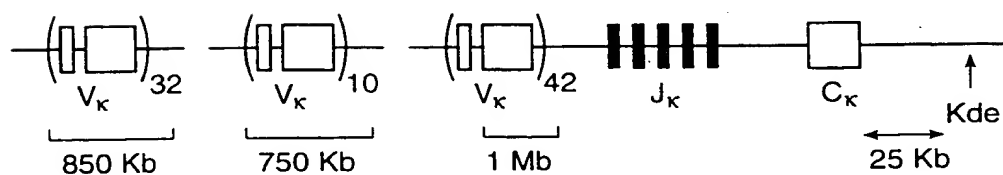


FIG. 3

V REGION
(~2000 Kb)

CONSTANT REGION
(~300 Kb)

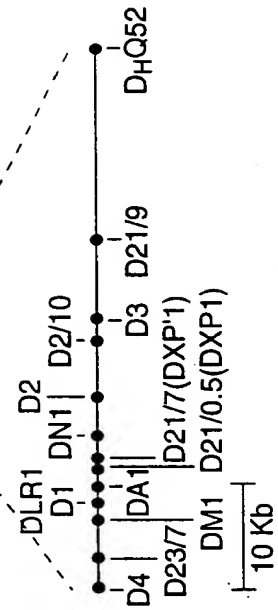
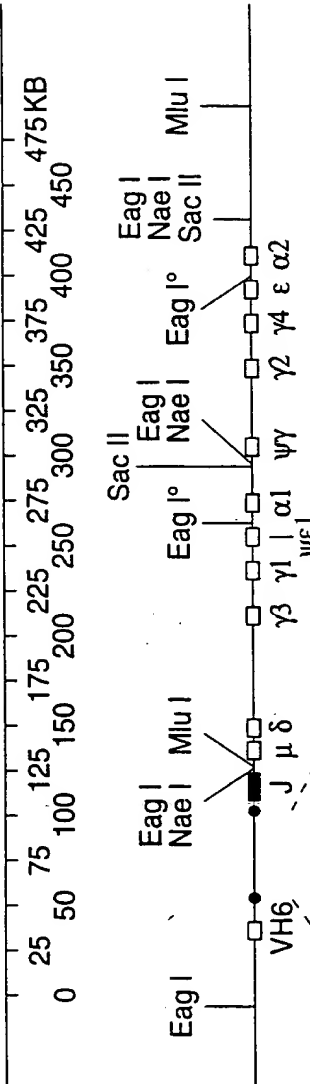
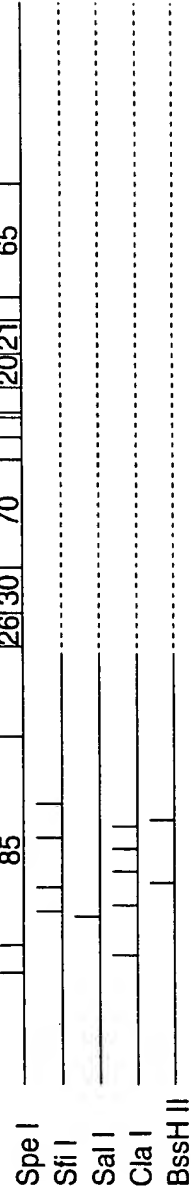
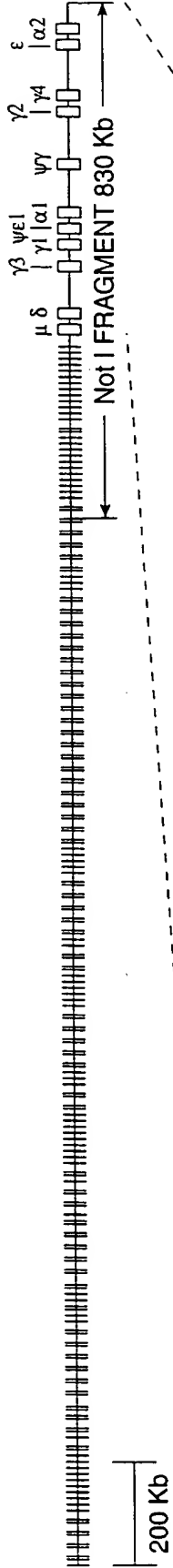


FIG. 4

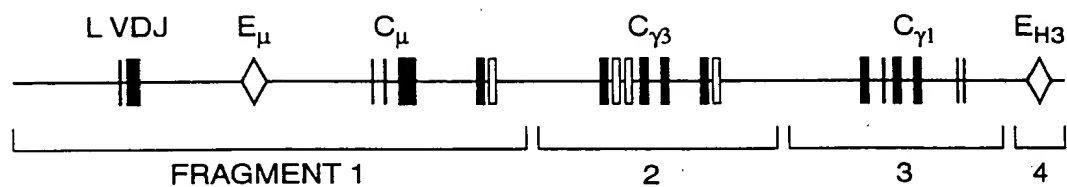


FIG. 5

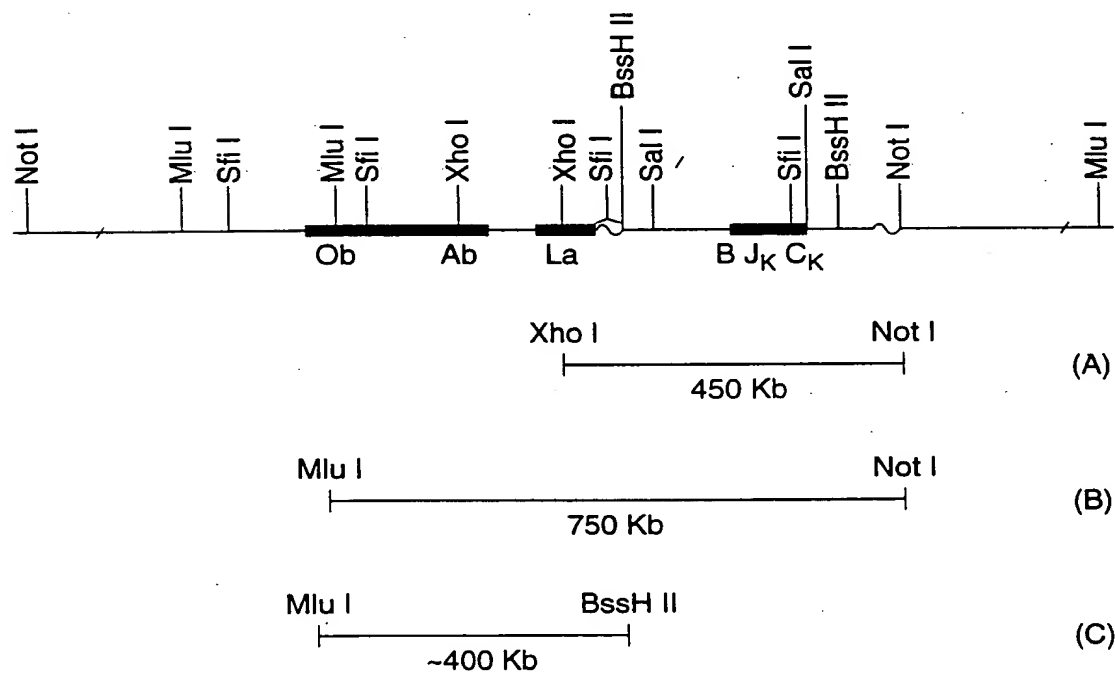


FIG. 6

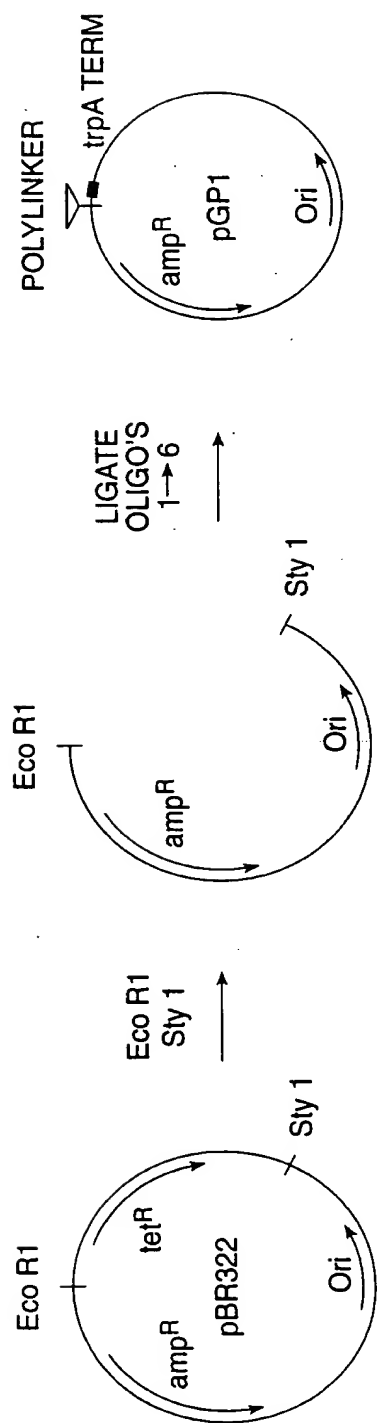


FIG. 7



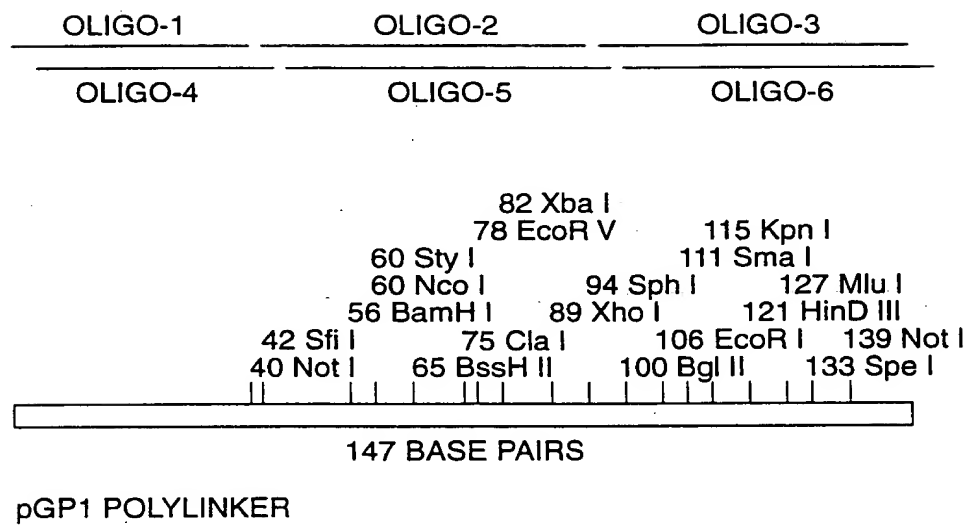
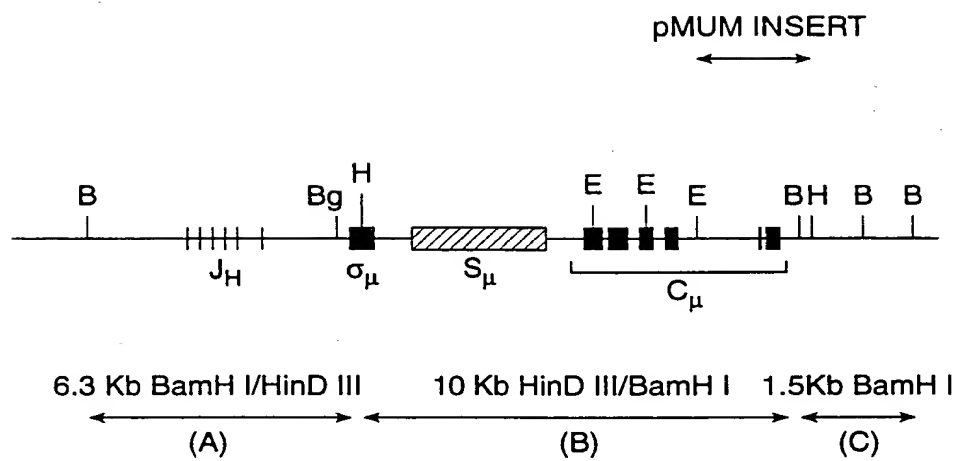


FIG. 8



HUMAN μ LOCUS

FIG. 9

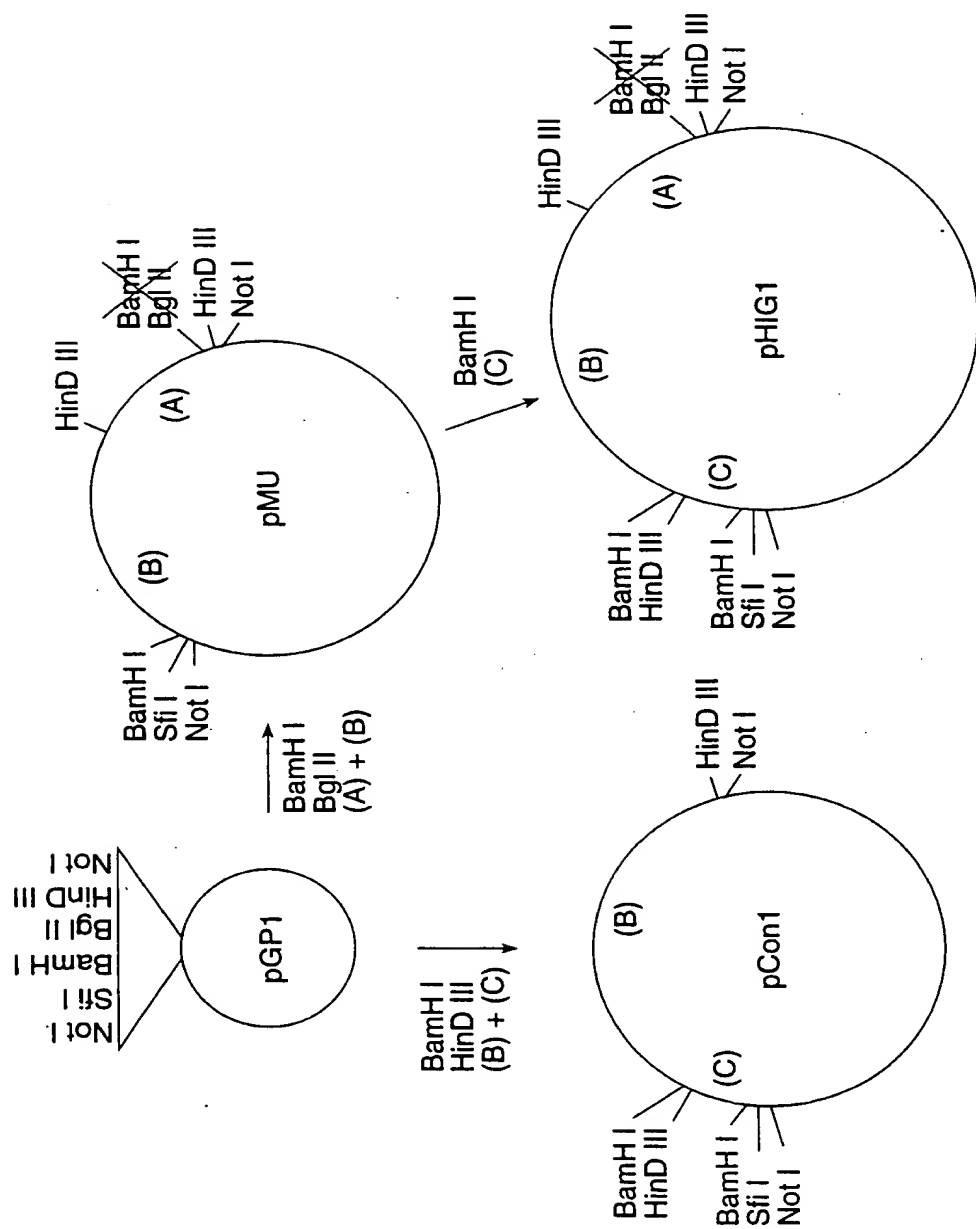


FIG. 10

HUMAN C_{γ1} GENE

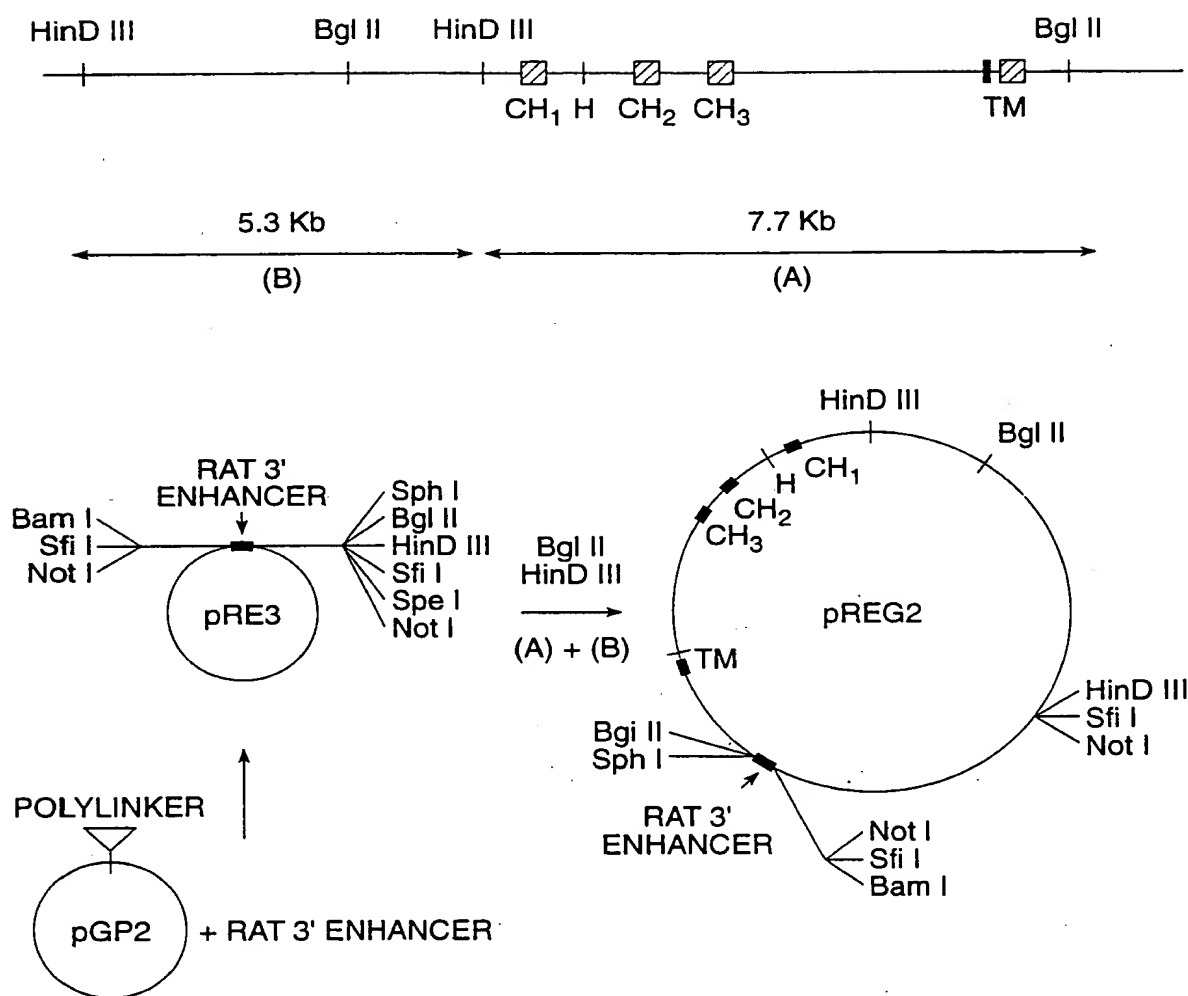


FIG. 11

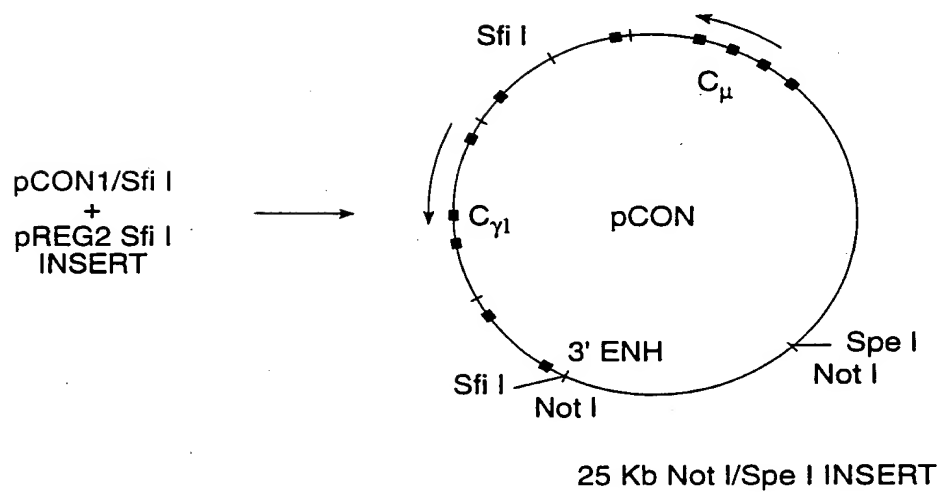
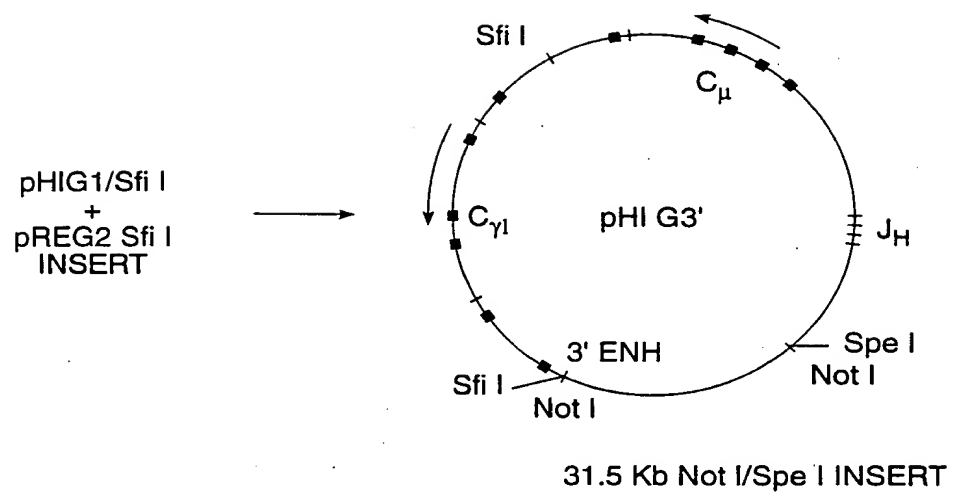


FIG. 12

HUMAN D REGION

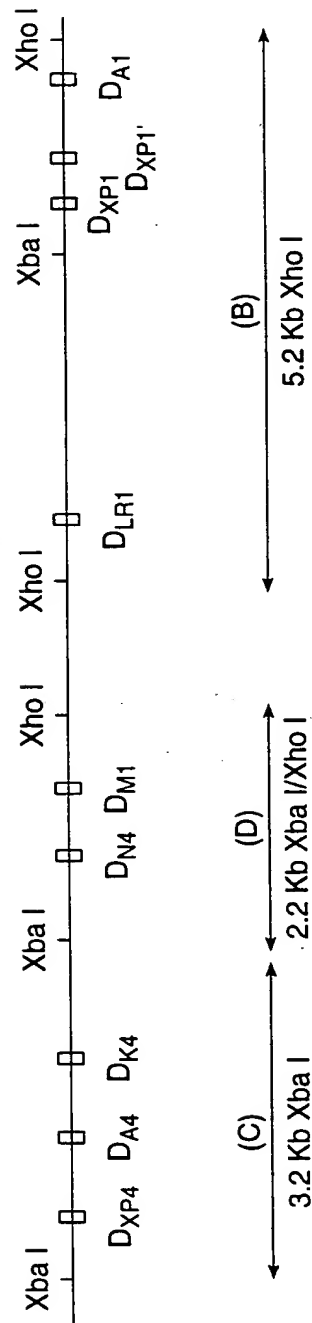


FIG. 13

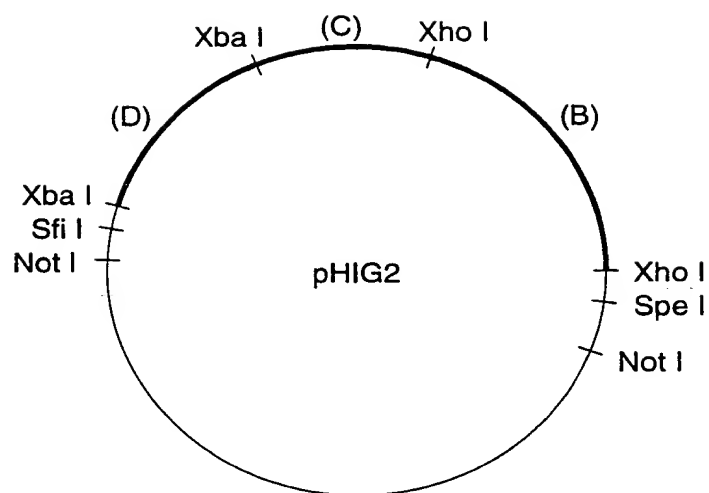


FIG. 14

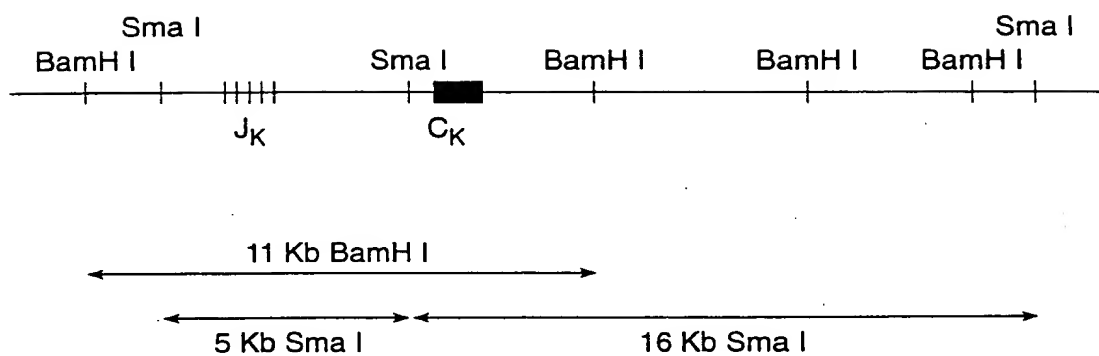


FIG. 15

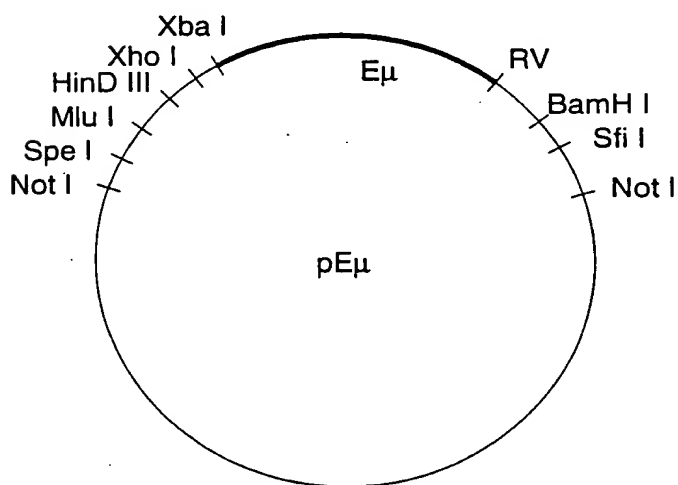


FIG. 16

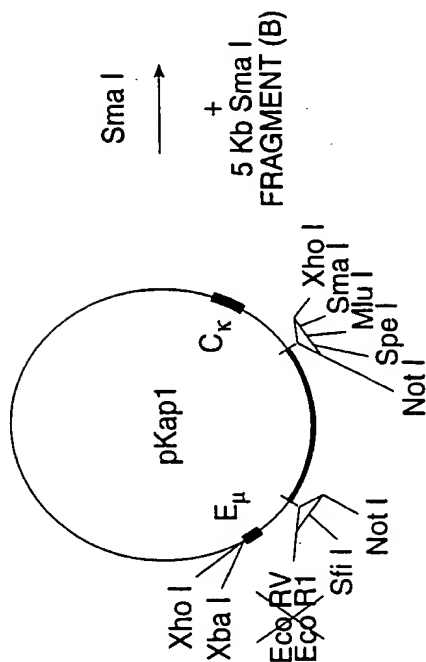
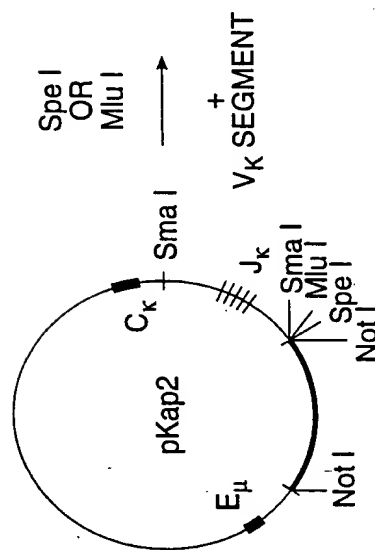
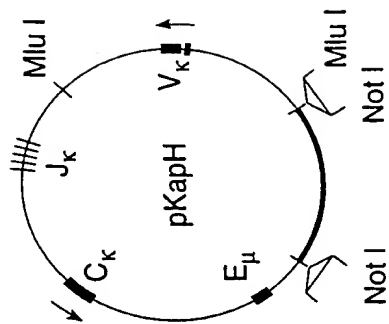


FIG. 17

MOUSE HEAVY CHAIN LOCUS

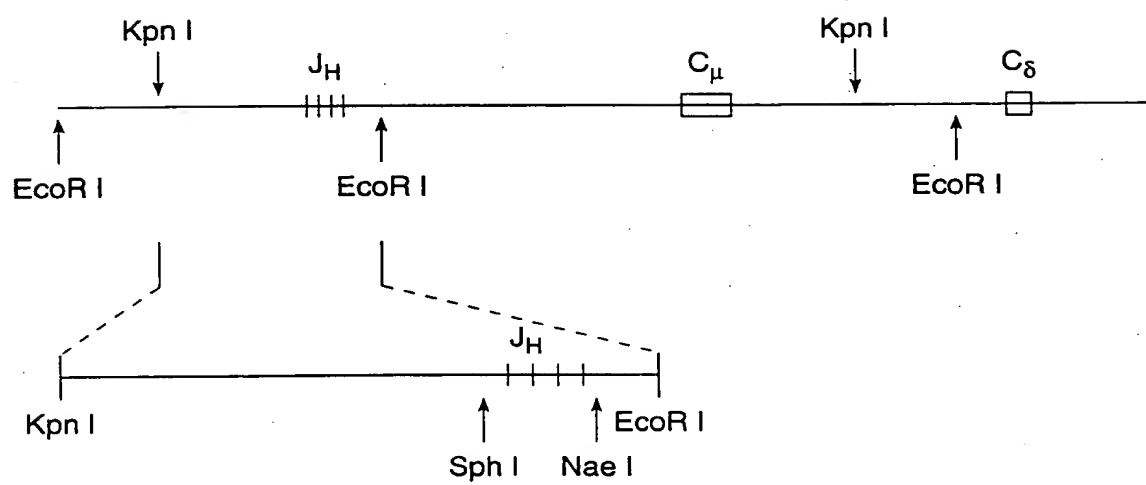


FIG. 18A

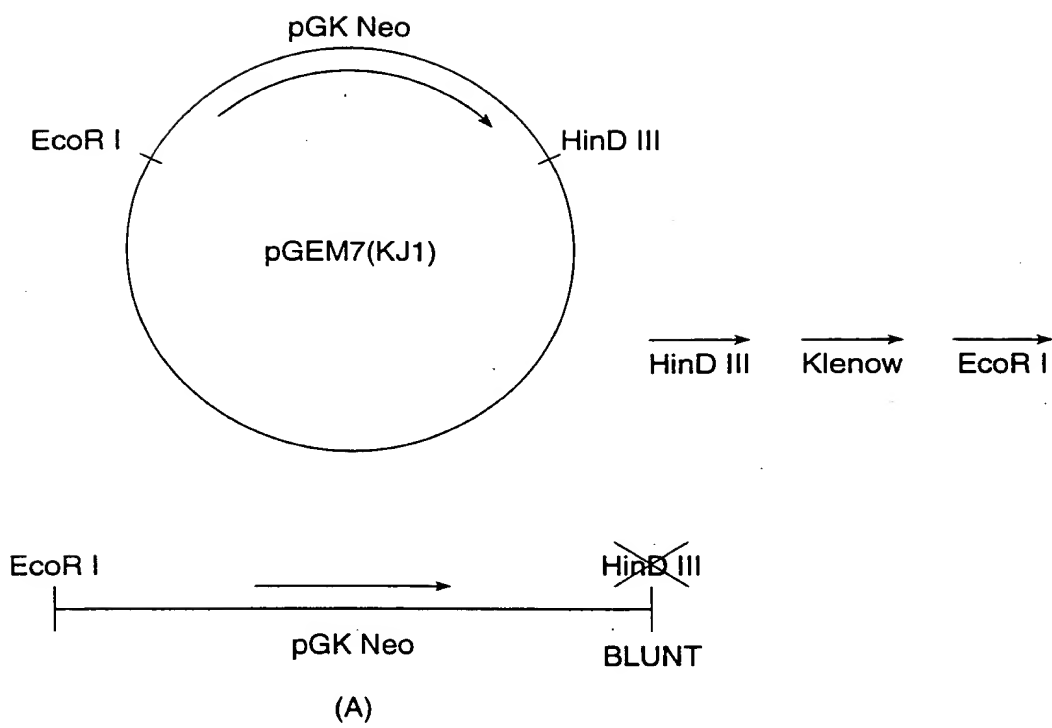


FIG. 18B

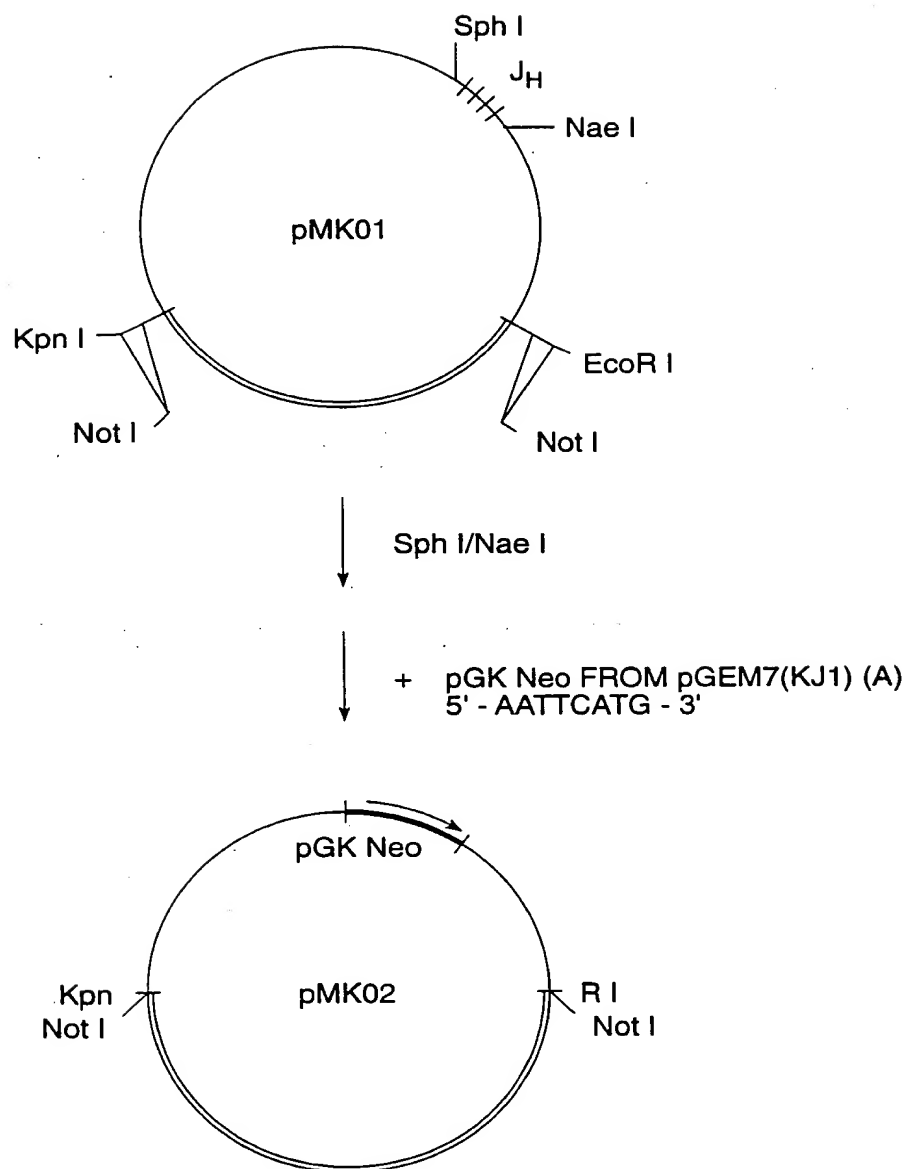


FIG. 18C

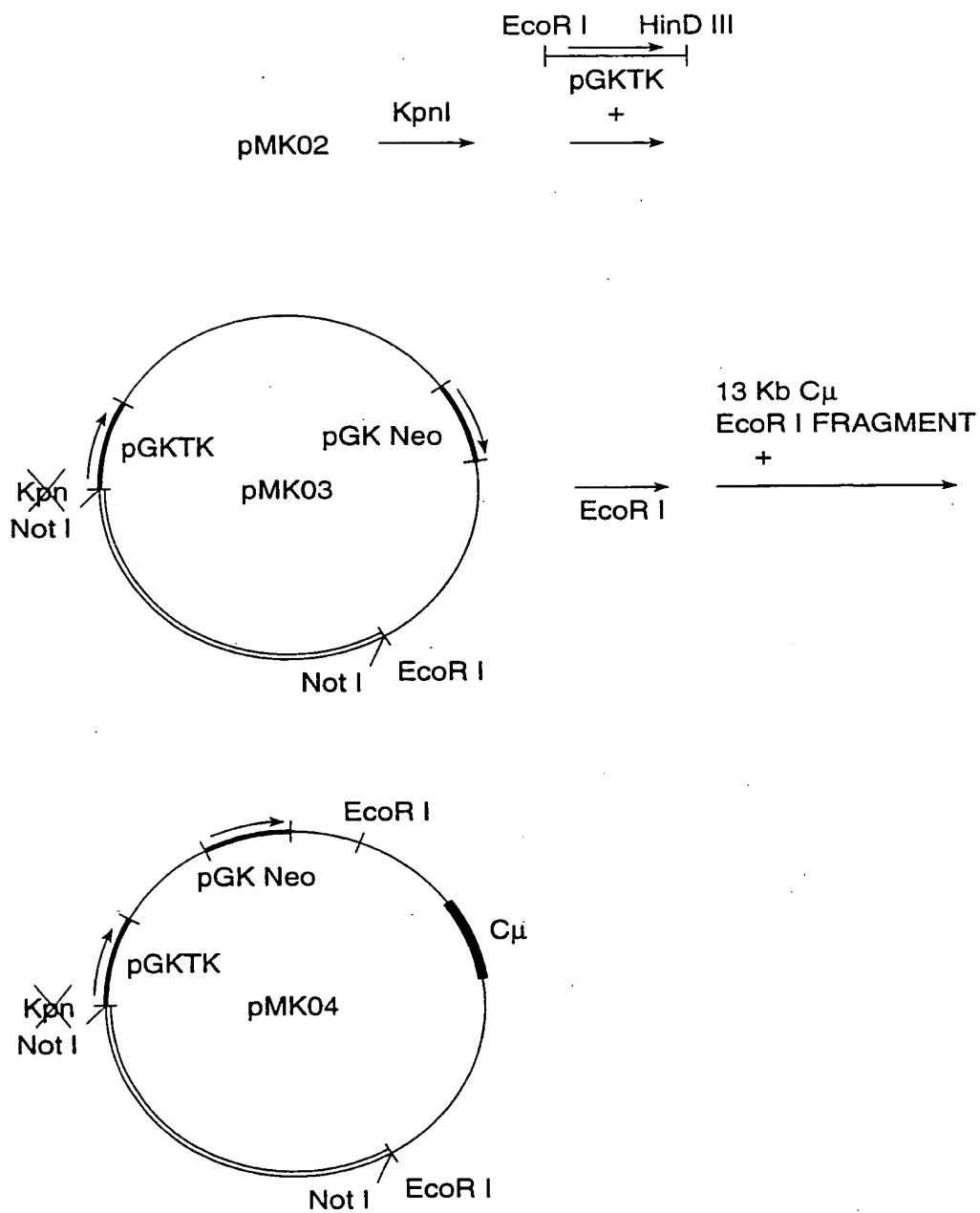


FIG. 18D

MOUSE KAPPA GENE

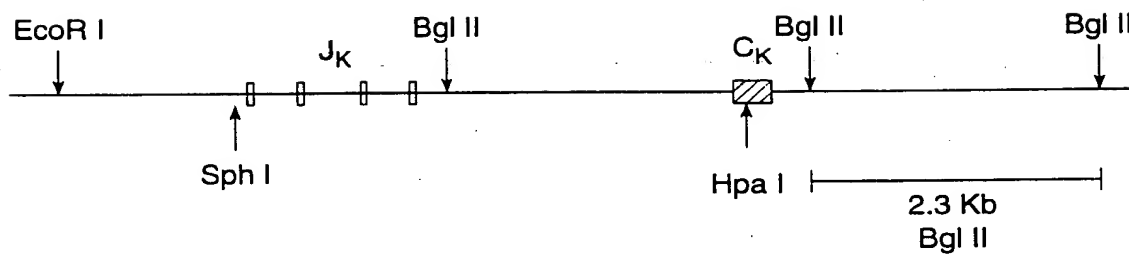


FIG. 19A

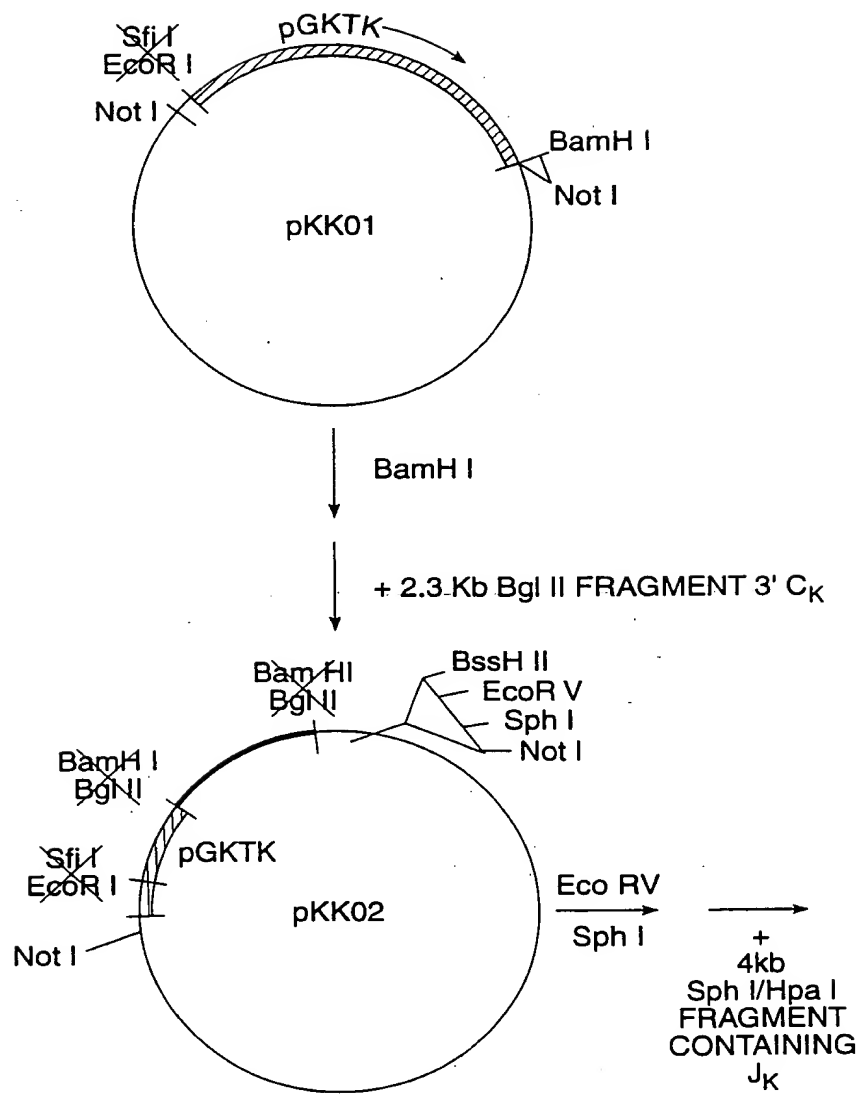


FIG. 19B

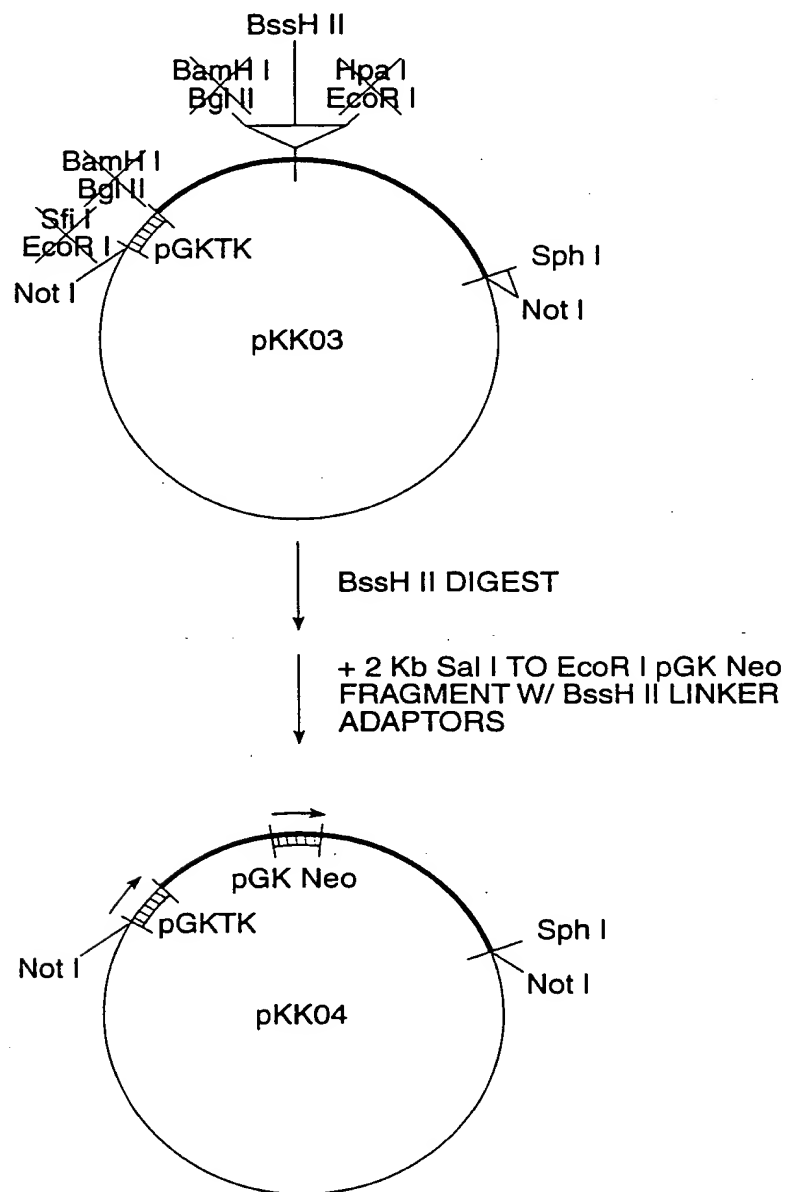
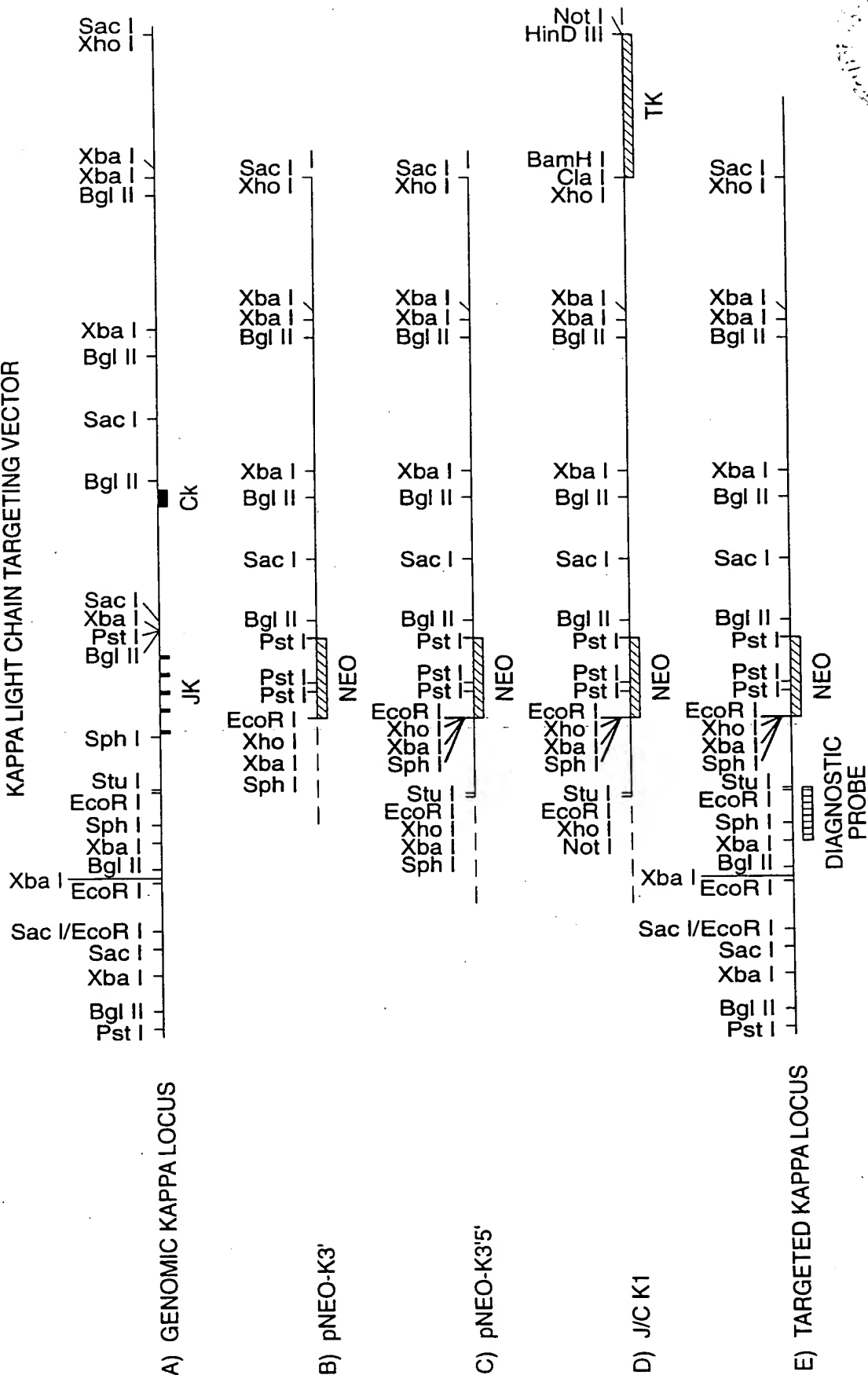


FIG. 19C

KAPPA LIGHT CHAIN TARGETING VECTOR



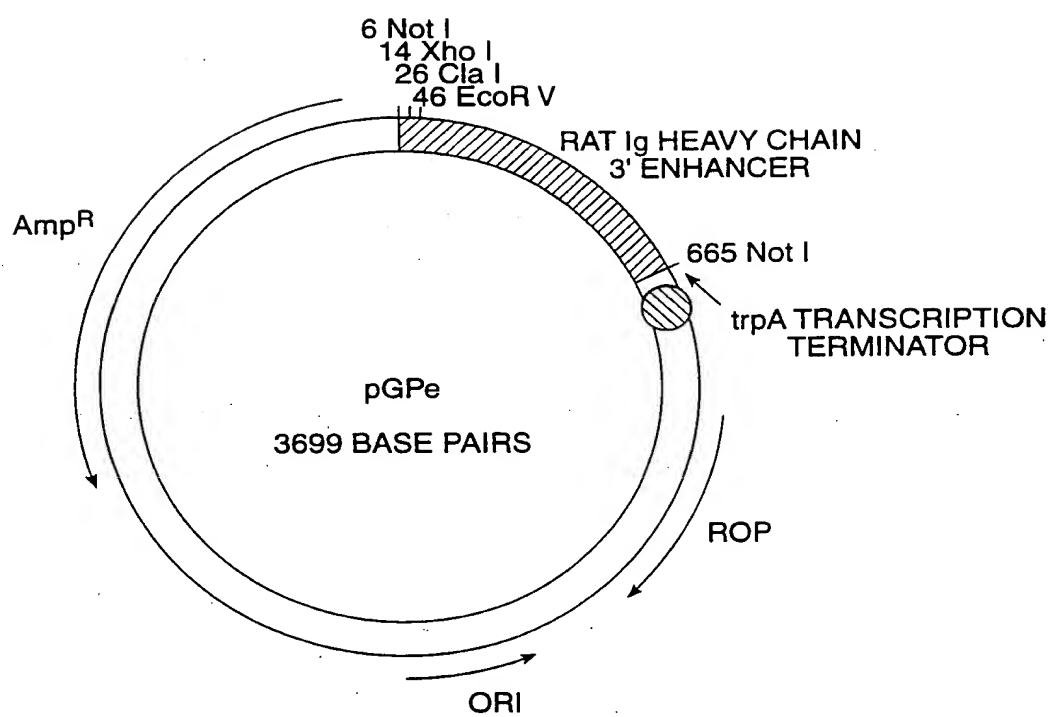


FIG. 22

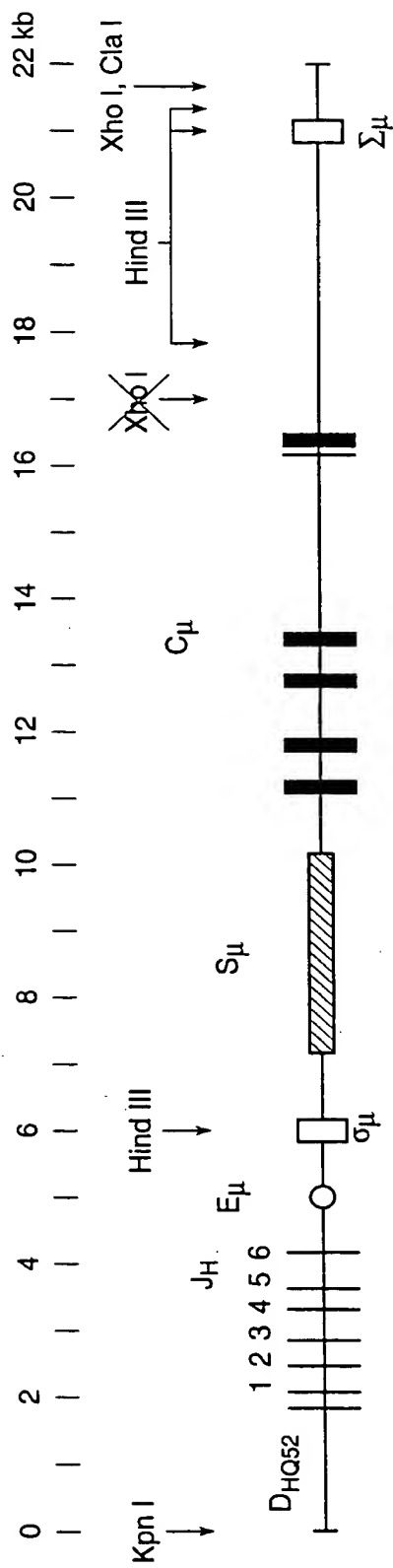


FIG. 23

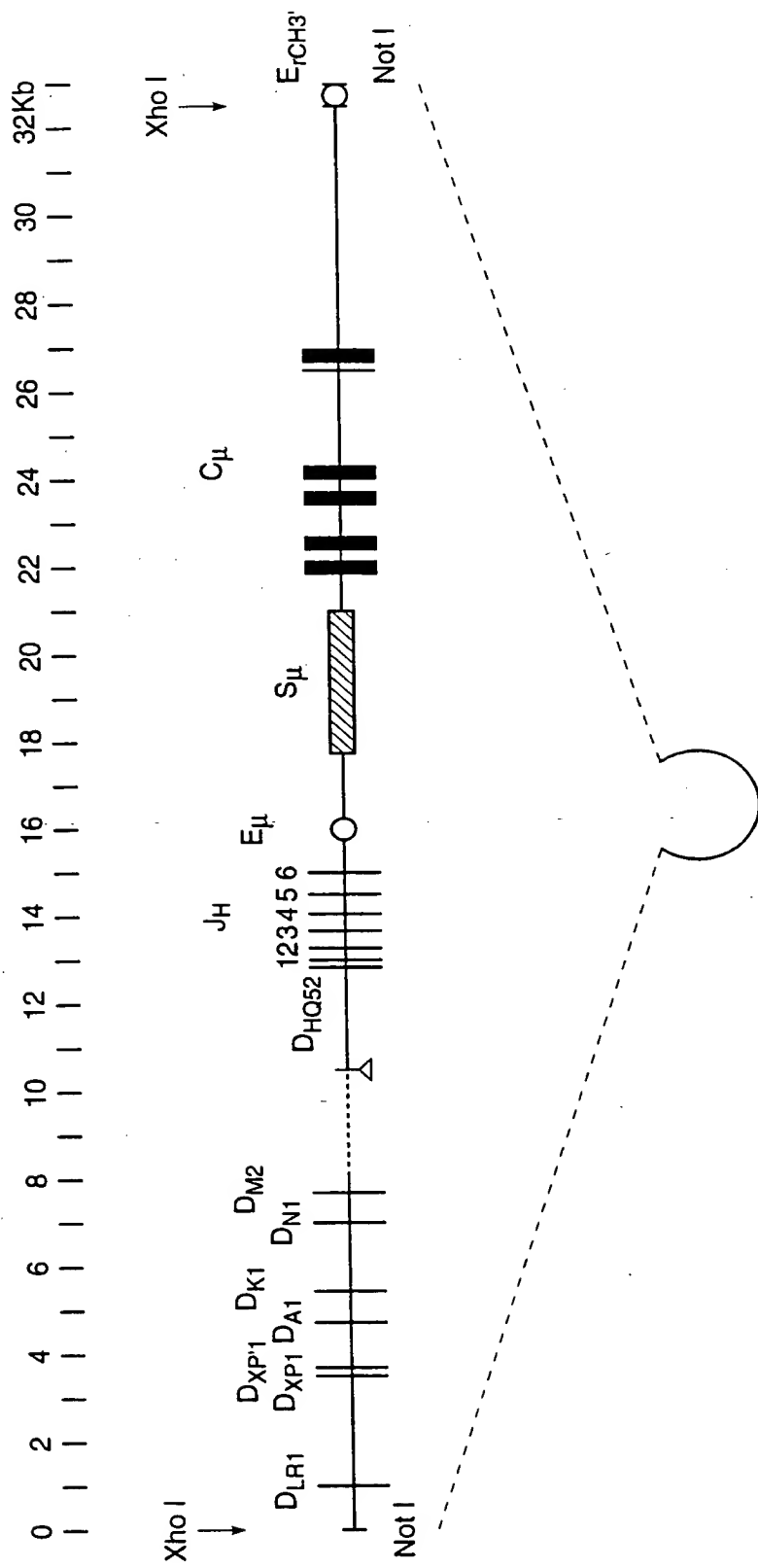


FIG. 24

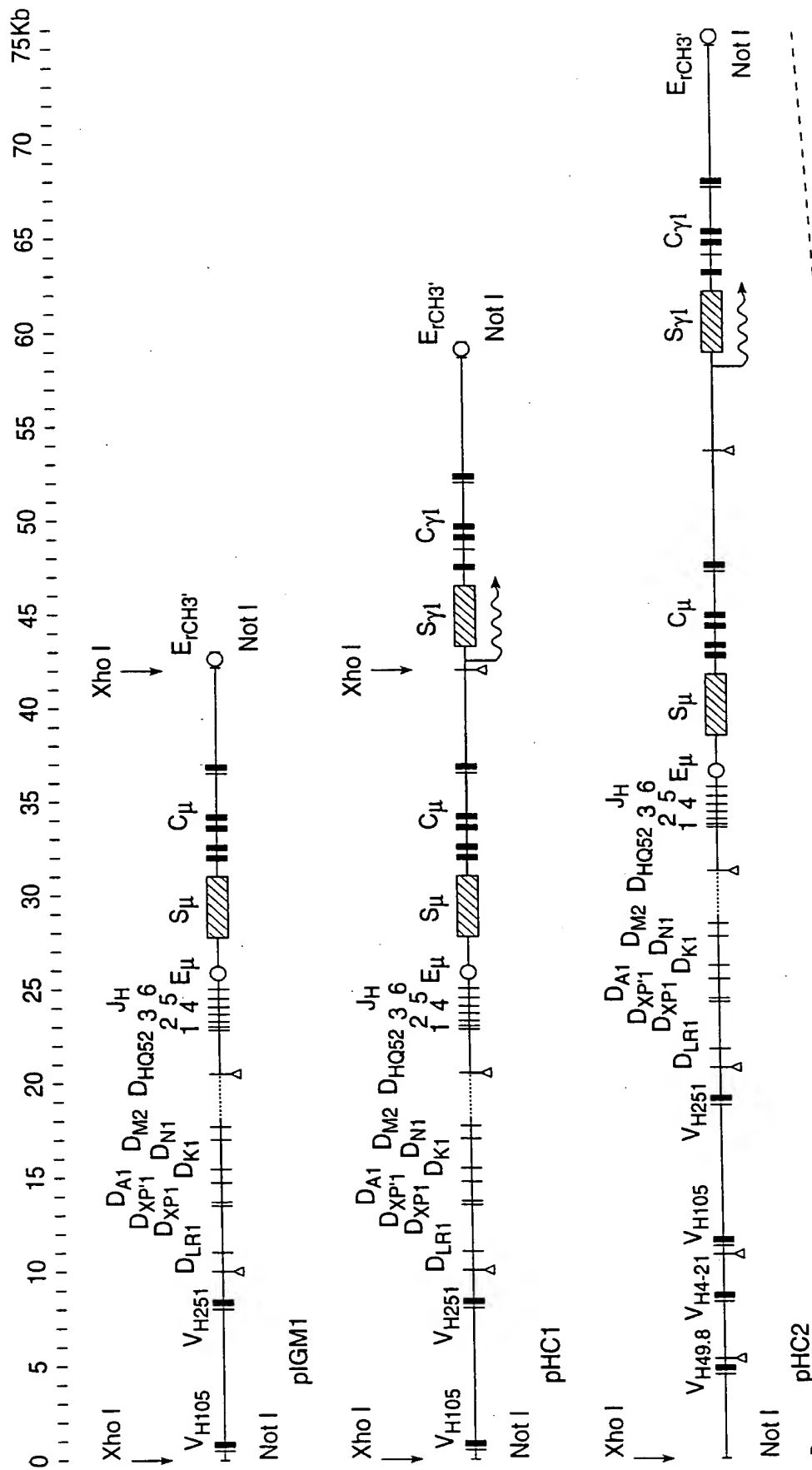


FIG. 25

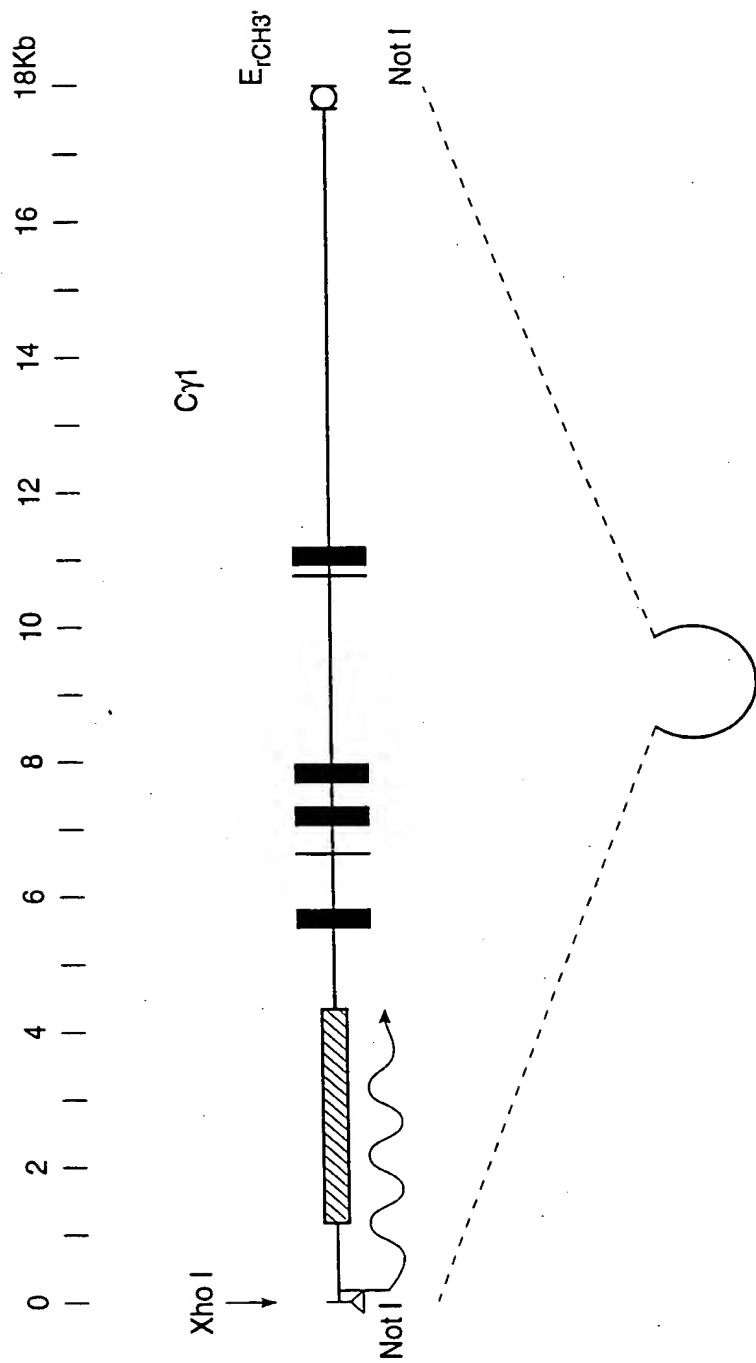


FIG. 26

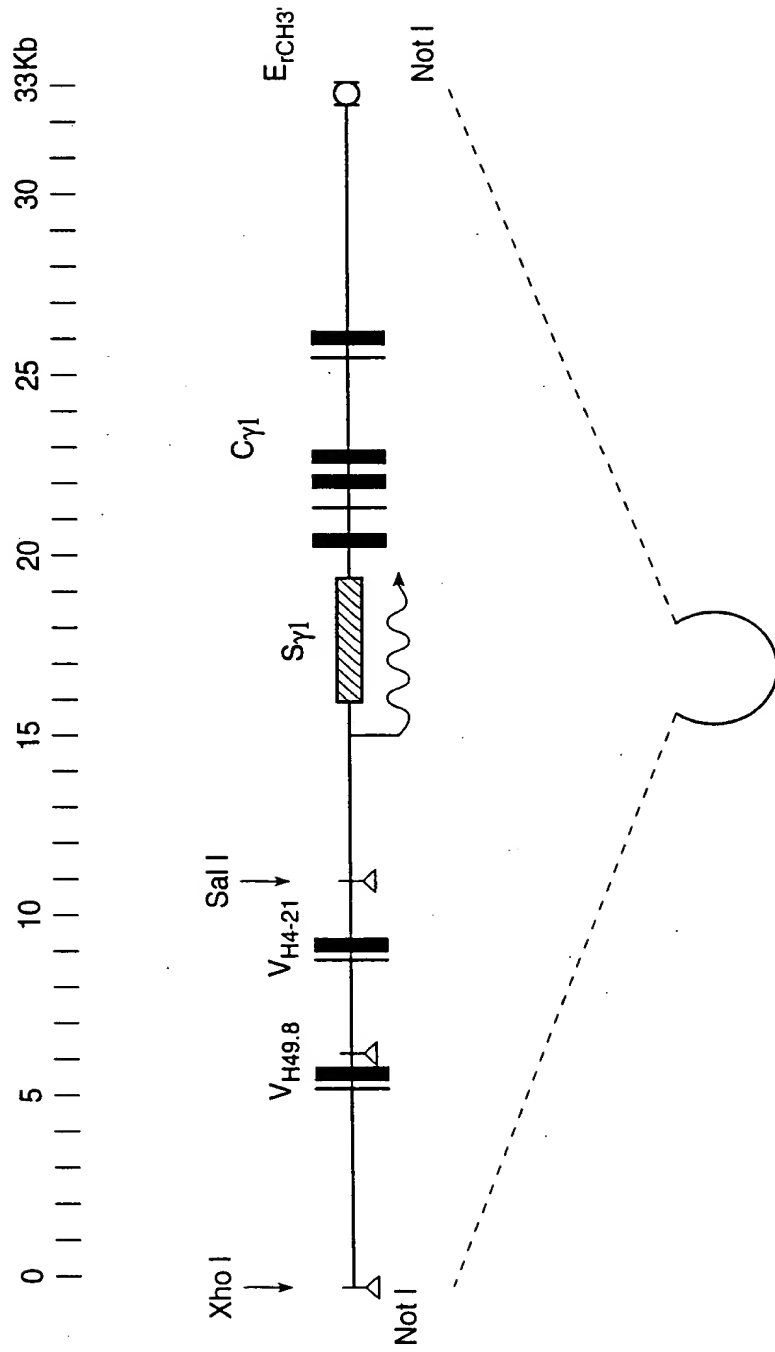
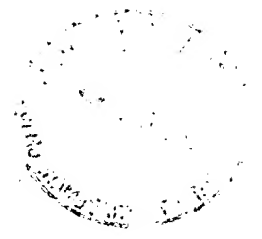
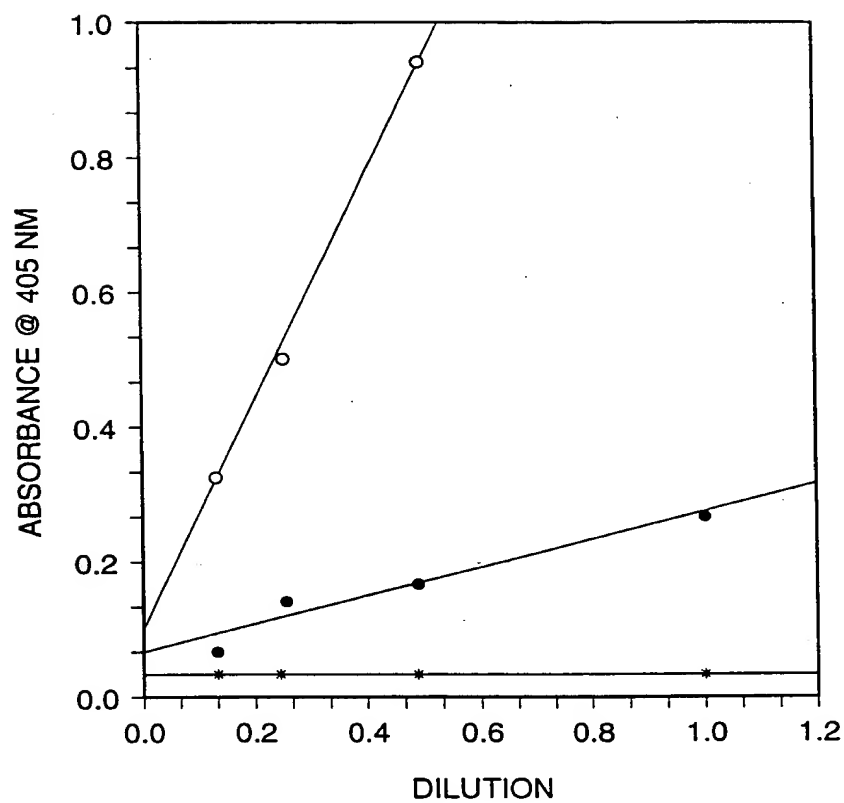


FIG. 27





○ IgM } pHc1 TRANSGENIC
● IgG1 }
× IgM } NON-TRANSGENIC CONTROL
+ IgG1 }

FIG. 28

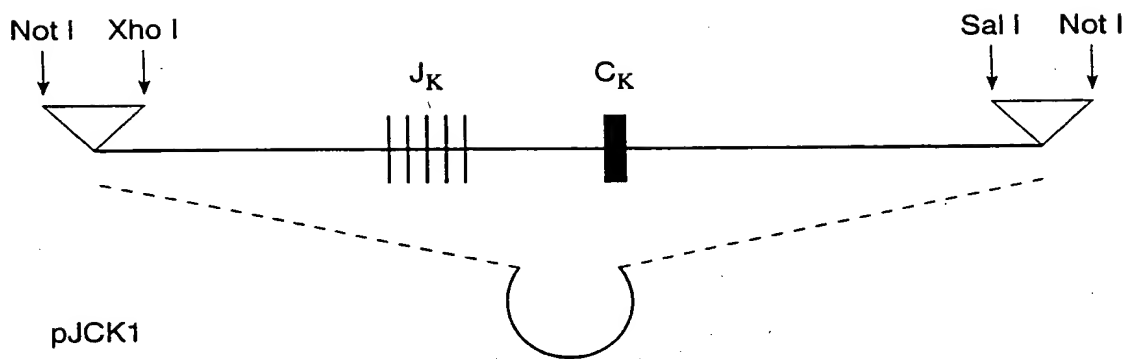
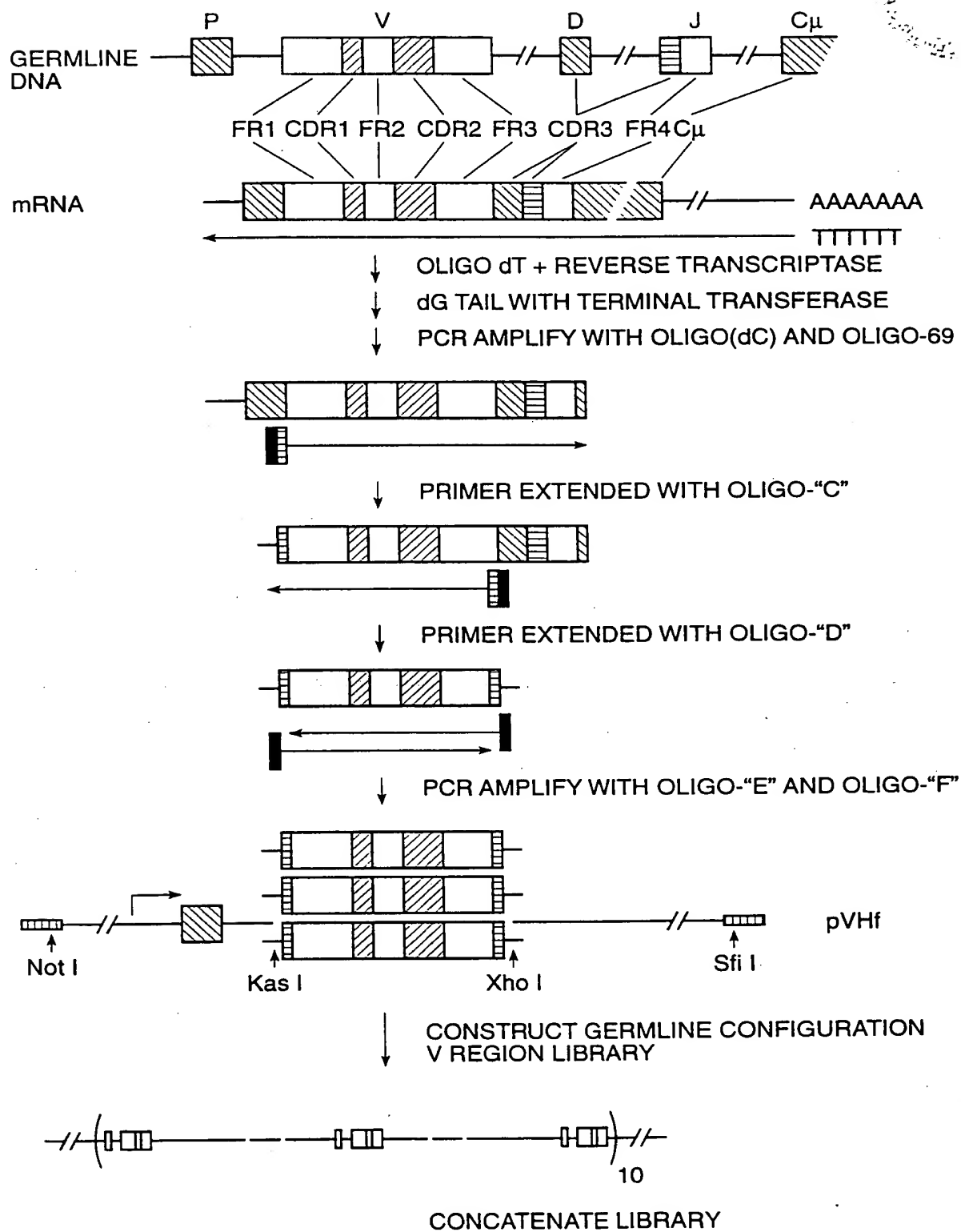


FIG. 29



SYNTHETIC HEAVY CHAIN VARIABLE REGION

FIG. 30

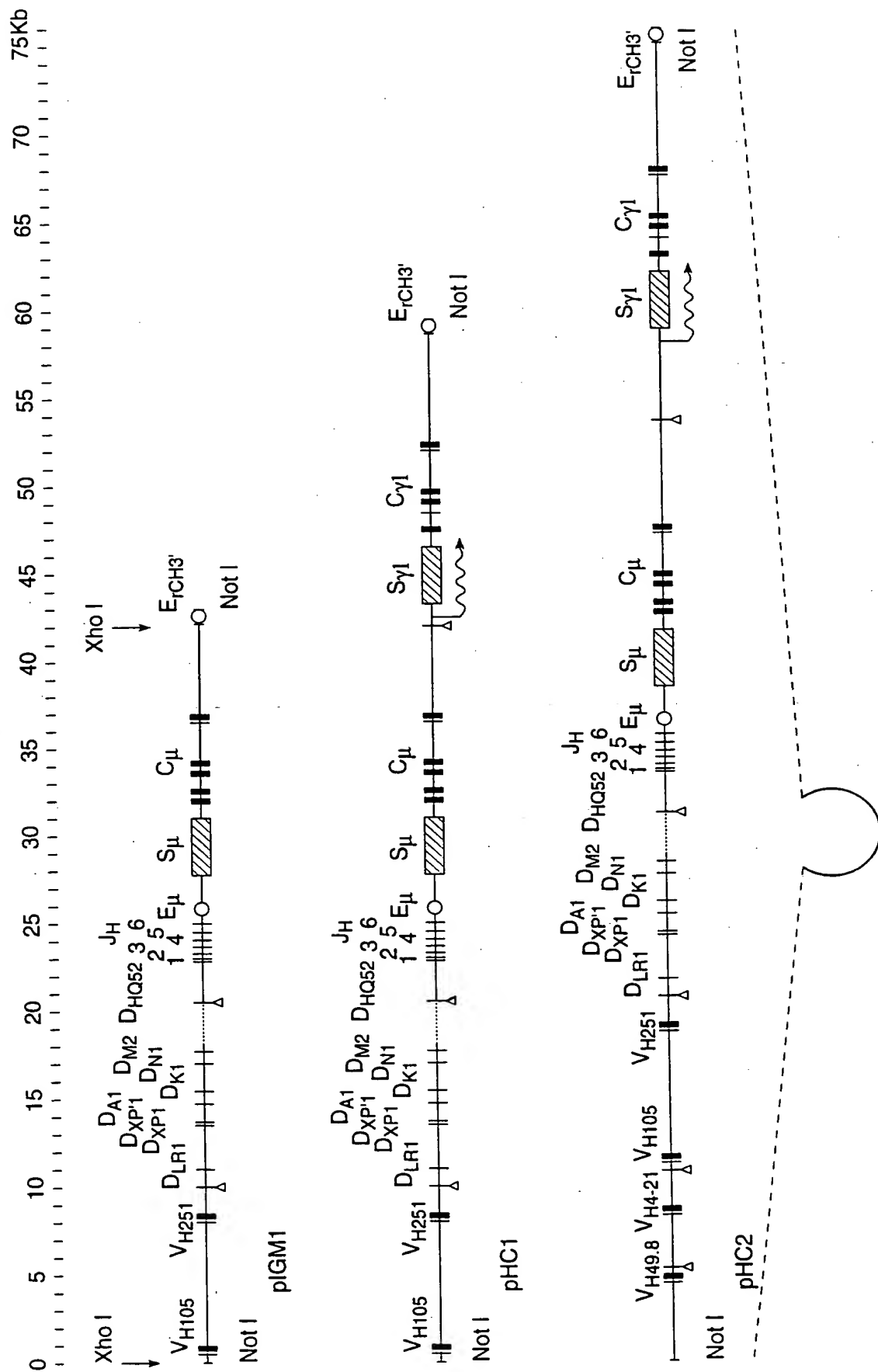


FIG. 31

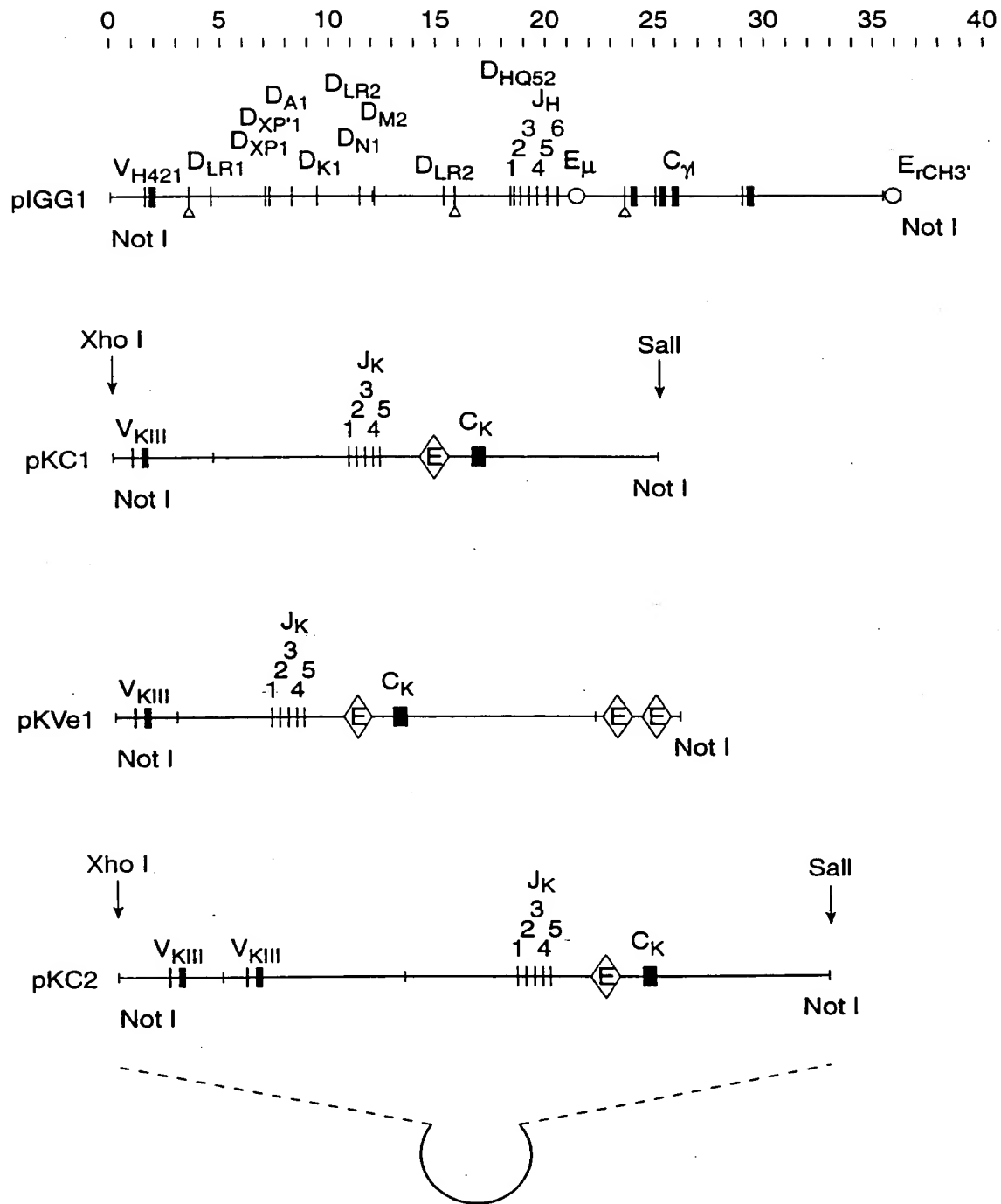


FIG. 32

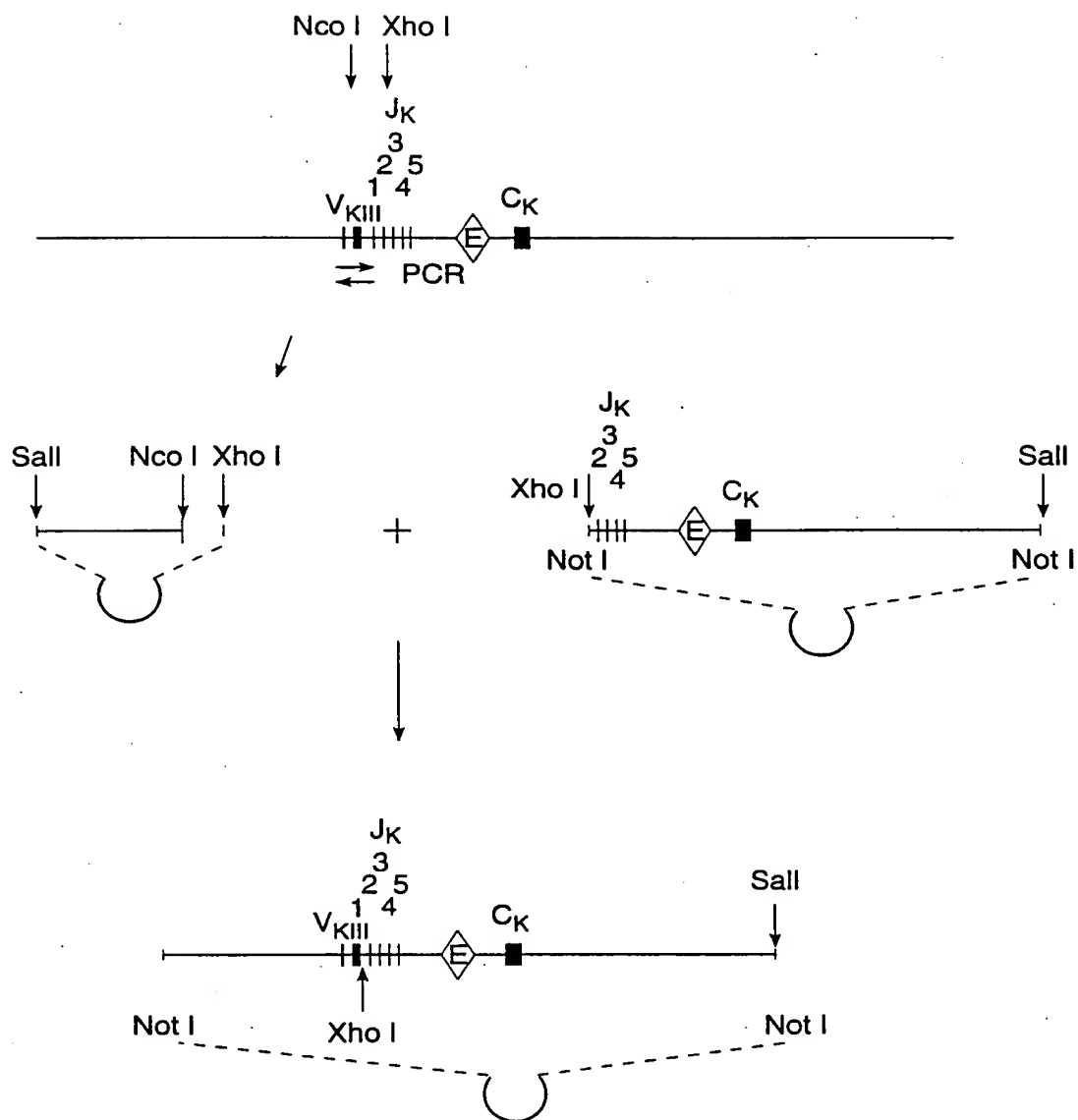


FIG. 33

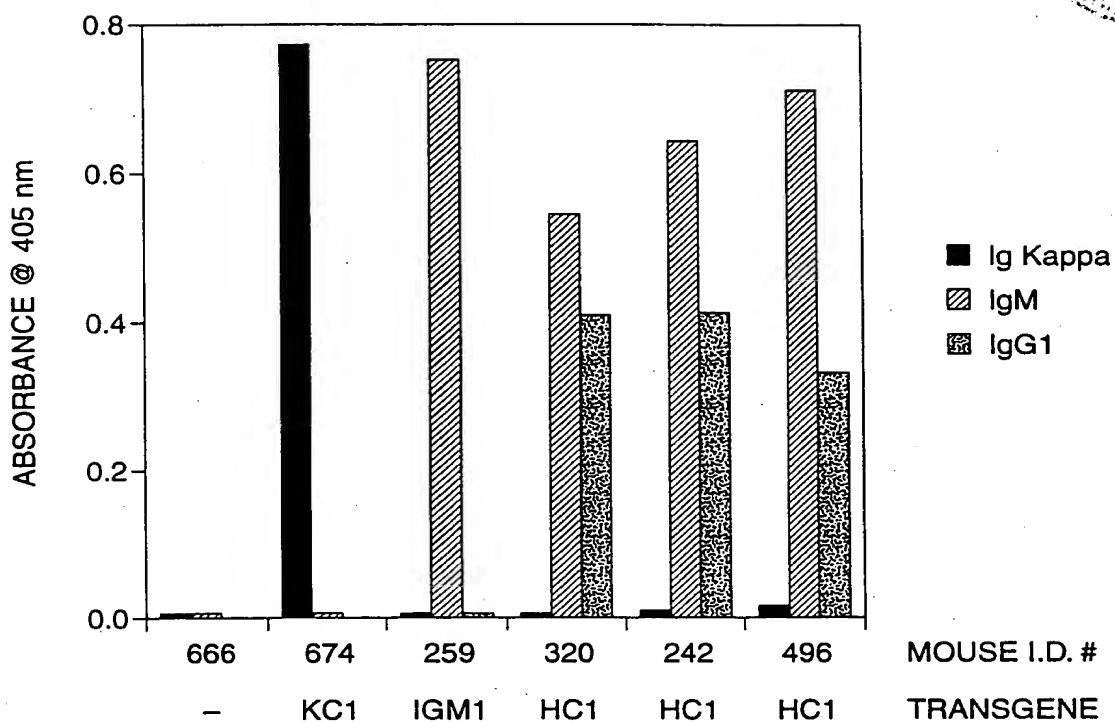


FIG. 34

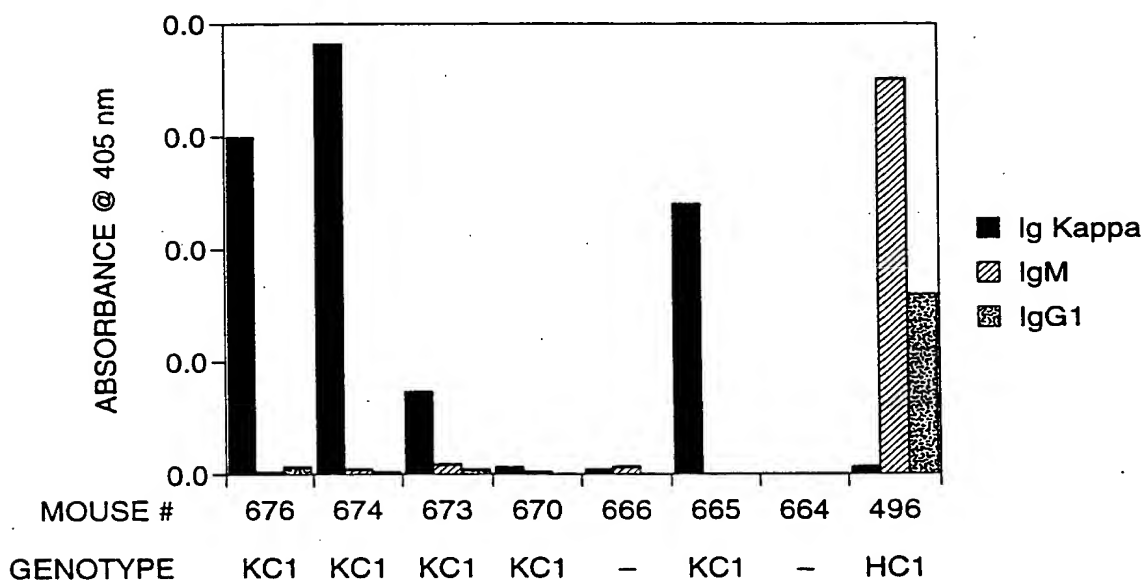


FIG. 35

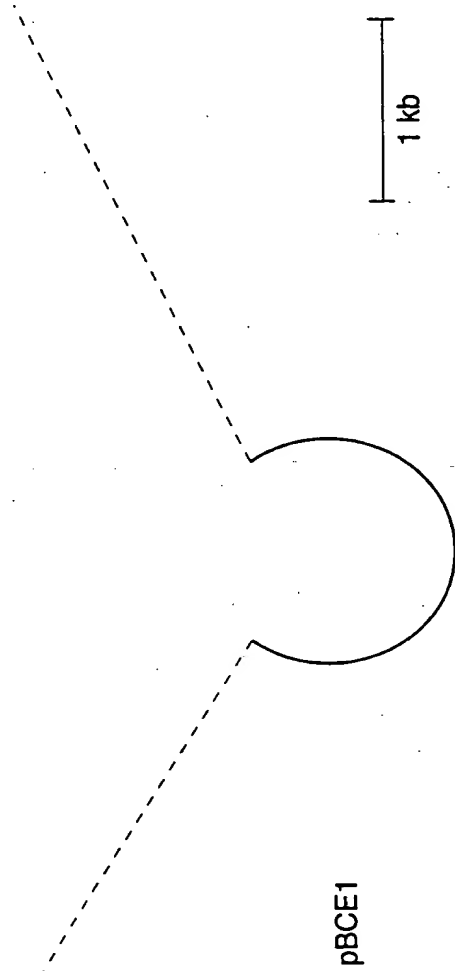
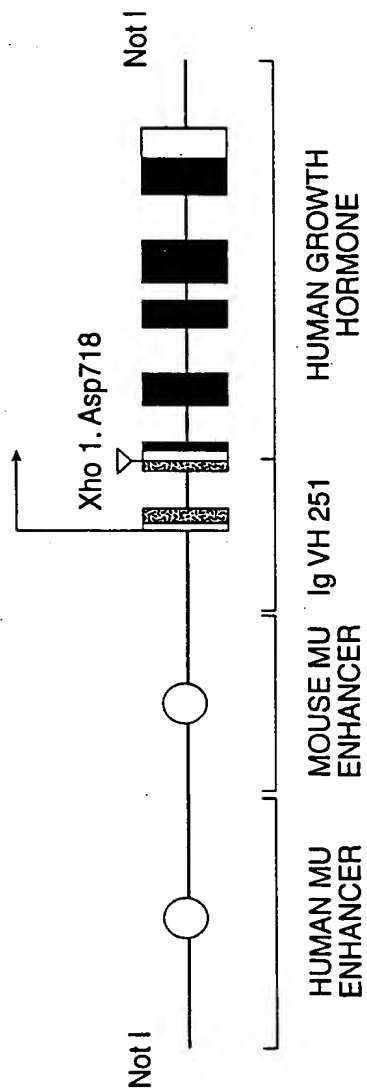


FIG. 36

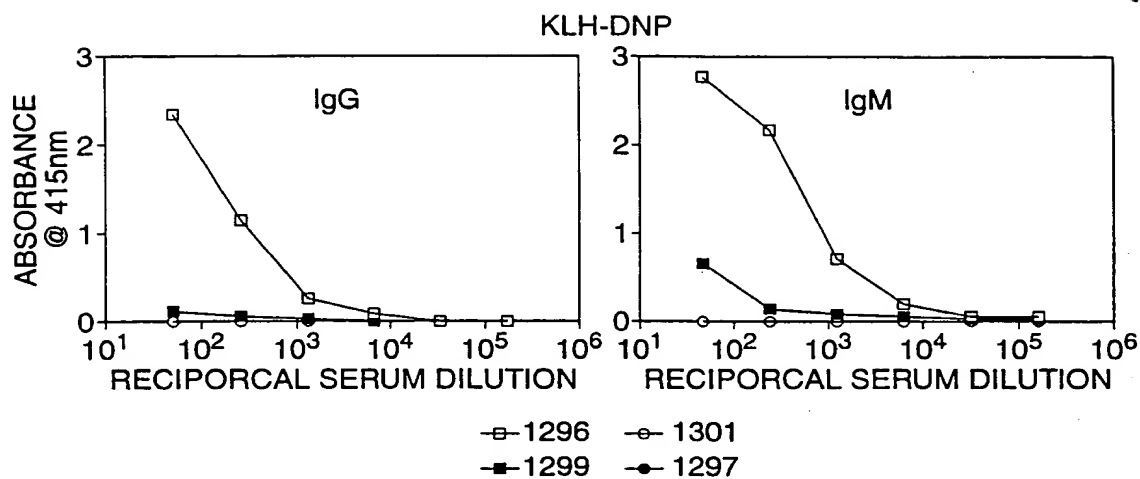


FIG. 37A

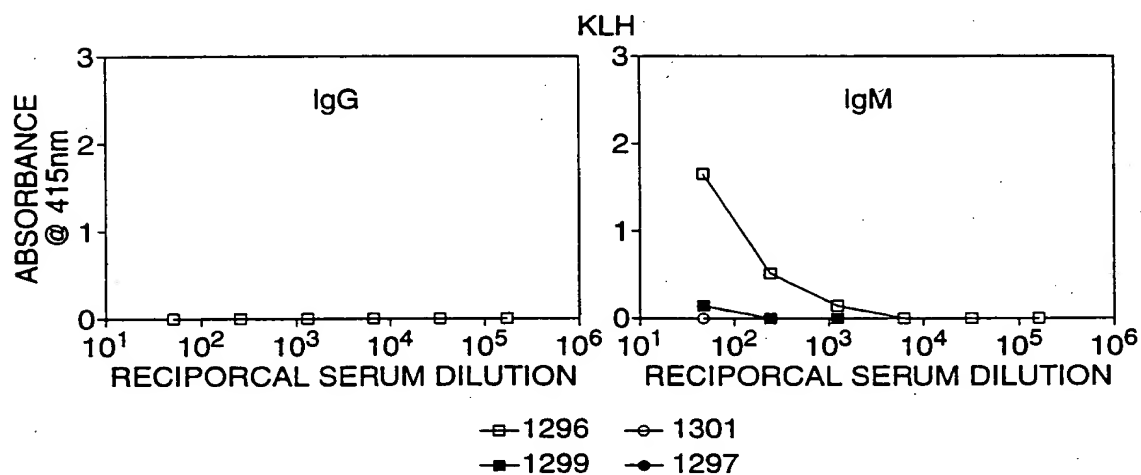


FIG. 37B

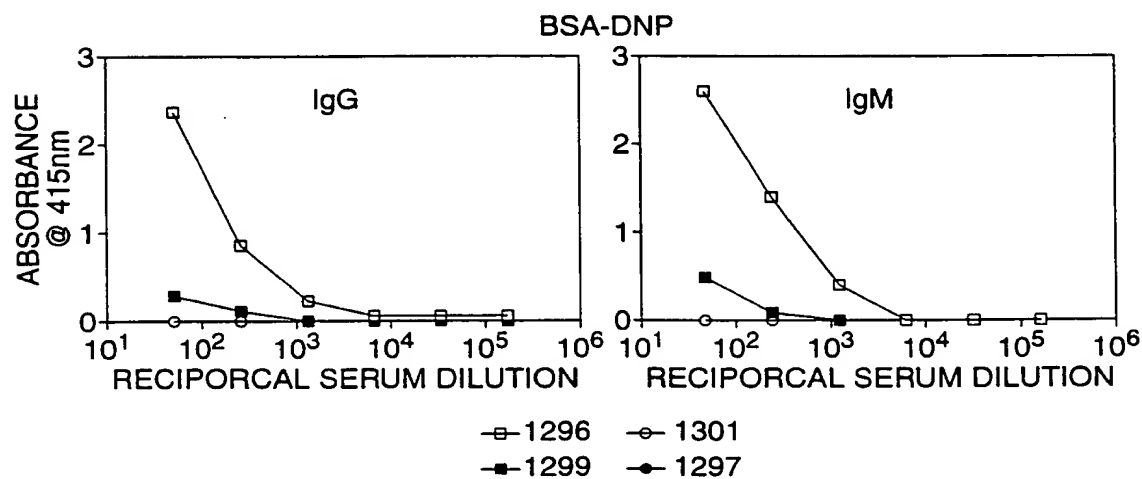


FIG. 37C

- HC1-26 HUMAN Ig
MINILOCUS TRANSGENE
(POOLED SERUM
FROM 3 MICE)
- HC1-57 HUMAN Ig
MINILOCUS TRANSGENE
(POOLED SERUM
FROM 3 MICE)

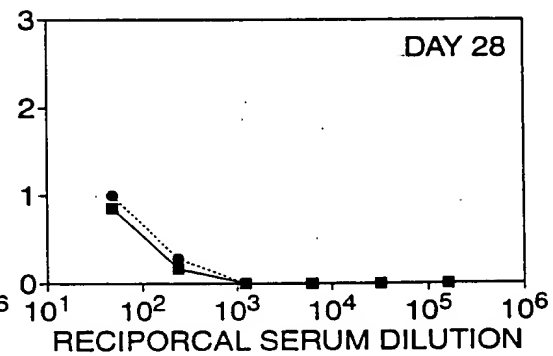
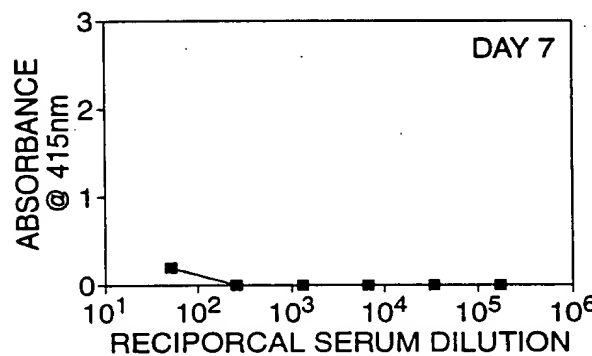
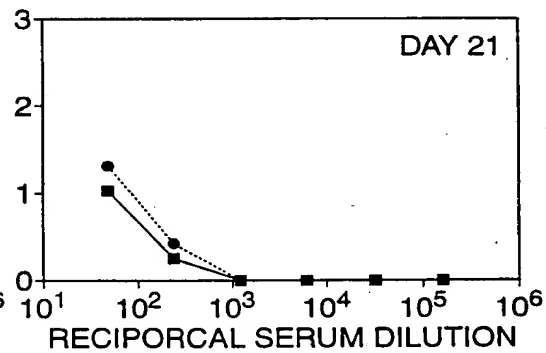
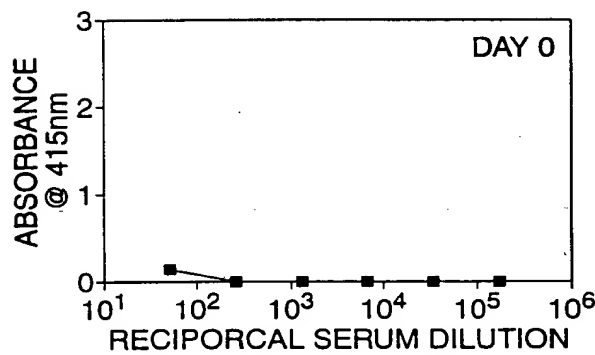
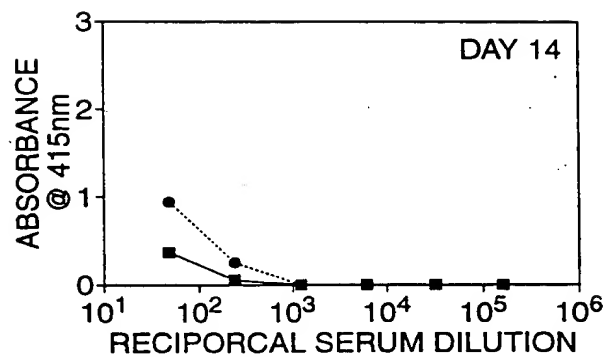


FIG. 38

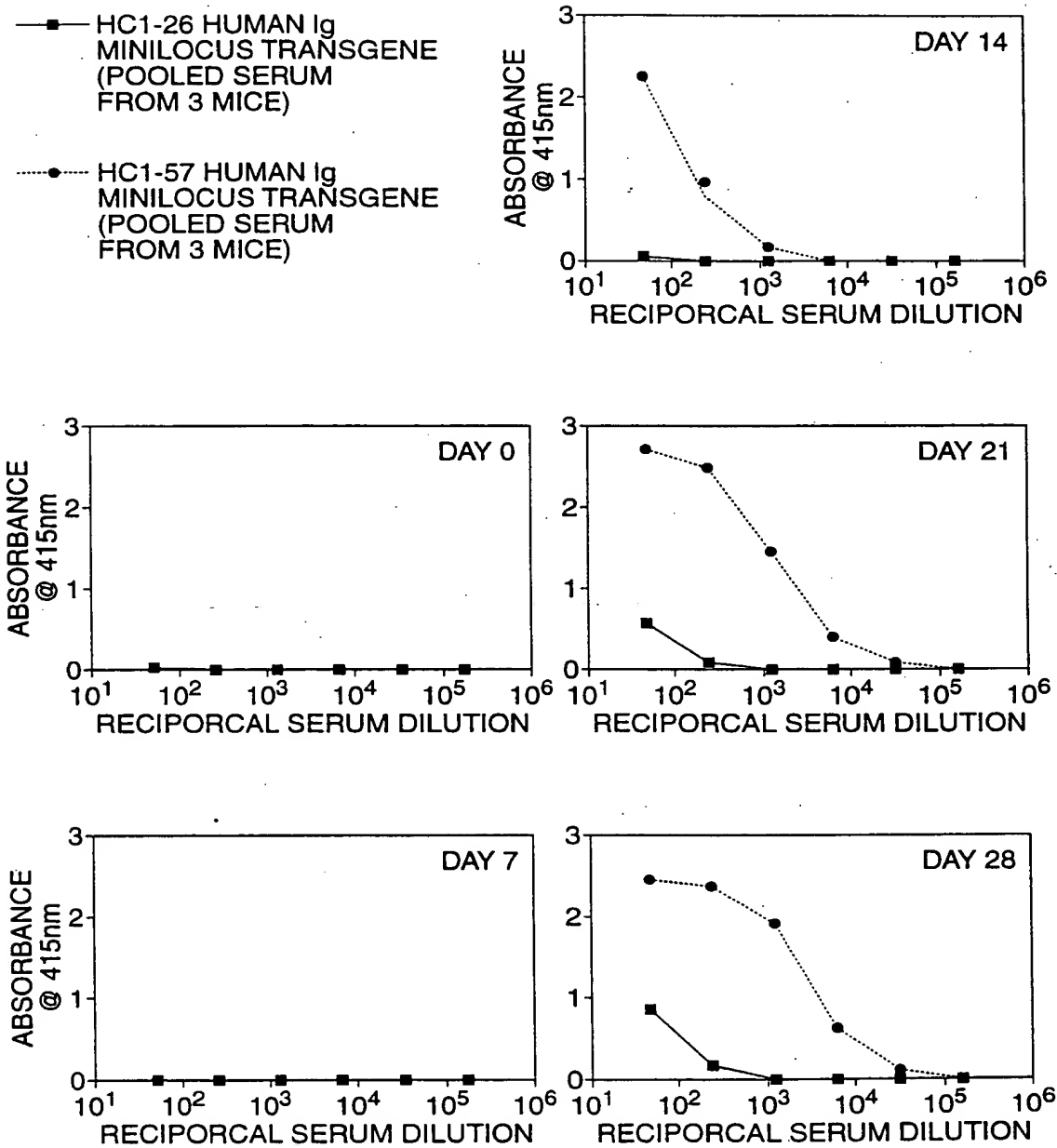


FIG. 39

2030

G.L. TCTCTGAAGATCTCCTGTAAGGGTTCTGGATACAGCTTTACCAGCTACTGGAT

J2.

5.C.....

J3.

10.

24.

J4.

32.C...T.....

1.T...T..GA.....

2.

3.

6.T...G.....

23.

30.

4.C.A.....

11.A.....

17.

27.

19.G.....T...T.....

34.T.....A...T..T.....

36.

J5.

25.A.....C.....

35.

J6.

18.A...T..C.....

22.C.....T.....

28.G...A.....

33.

CDR I

FIG. 40A

CGGCTGGGTGCGCCAGATGCCCCGGGAAAGGCCTGGAGTGGATGGGGATCATCTATCCTGGT

40

50

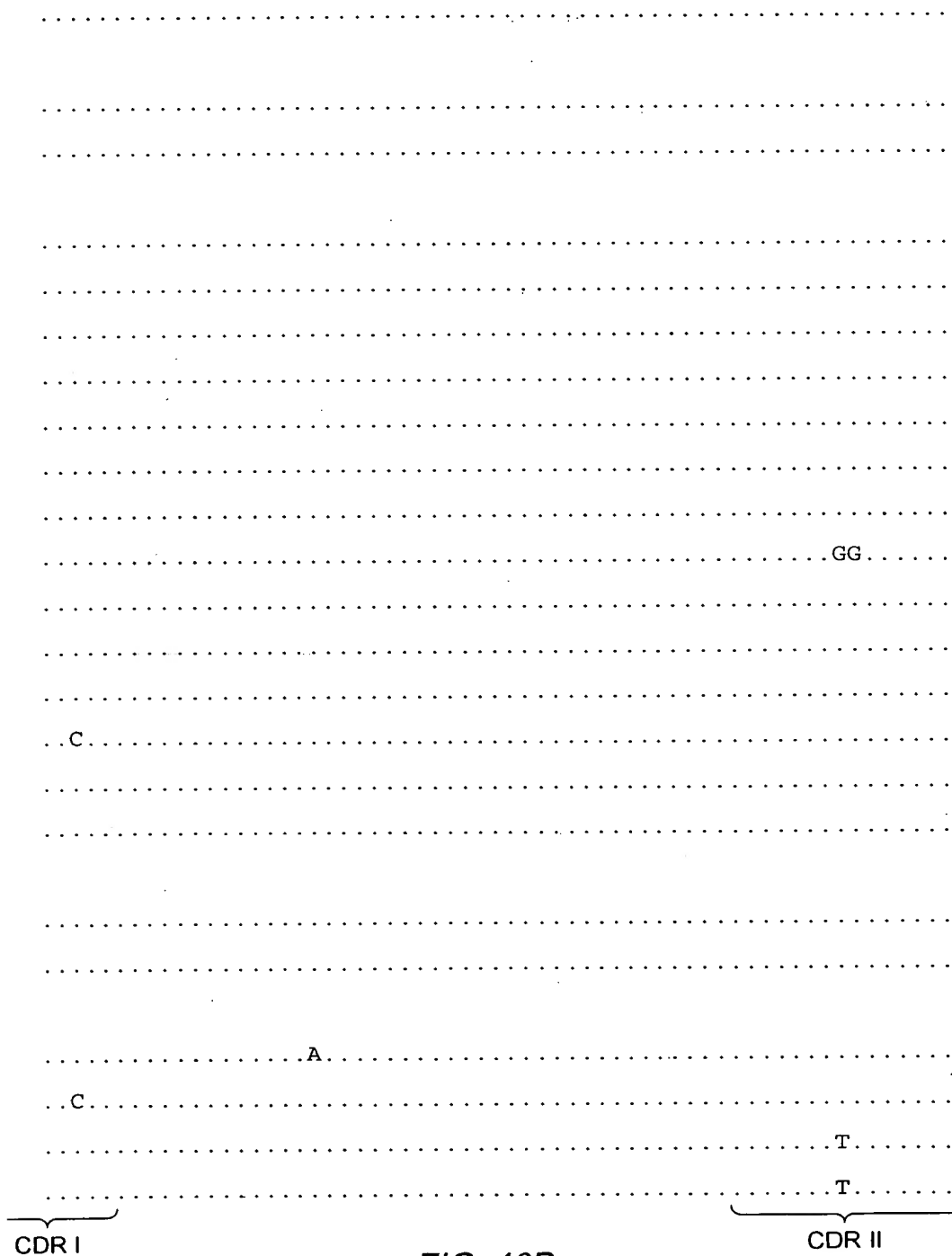


FIG. 40B

60
GACTCTGATACCAGATACAGCCCGTCCTTCCAAGGCCAGGTC

70
ACCATCTCAGC

.....G.....

.....

.....

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.....

.....C.....G.....

T.....T

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.....A.....T.....

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.....

.....

.....

.....

.....C.....

.....

.....

CDR II

FIG. 40C

80 90
CGACAAGTCCATCAGCACCGCCTACCTGCAGTGGAGCAGCCTGAAGGCCTCGGACACCGCC

.....CG.....
.....
.....G.....GT.T.
.....
.....A.....T.....A.C.....G.....T.....
.....
.....
.....
.....T.....G.....
.....
.....T.....
.....G.....
.....
.....
.....
.....
.....
.....
.....G.....
.....
.....
.....
.....C.....
.....A.....

FIG. 40D

ATGTATTACTGTGCGAGA

TACTGGTAC

.....CAGGGGGGGGATA.....
GCT
.....CATTGGctaaAtggggaT....
.....CGGGattacgatattttgactgggttattatGCG...
TAC
.....GtggttcggggaTttattatT...
.....GGgtattaTtatgAttcggggaCttattataaGTCTACCC...
.....ctaactggCCT...
.....CATCTT...
.....CATCTT...
..T.....CATCTT...
.....CG.....CATCTT...
.....CAAGGG
.....CAAACCT
.....CATggtatagcagcagctggtacgtgggttcGACCC
.....GCCgggtataCcagcagctggtT...
.....CAGGGC...
.....CAAAGGGG...
.....GGGATCGTGG...
AACTGG
.....CTCCCCAATGACAGT...
.....CGGGGGtactatggttcggggagttattat.....
TACTACTACTACTACGGT
.....CATGagcagctggtacAGGGT.....
.....GATATGGGGGGGGCCTC.....T.....T....
.....C..C..G.....
.....CG.....

CDR III

FIG. 40E

.....

.....

.....

.....T.....

.....A.....

.....A.....

.....

.....

.....

.....

.....

ATGGACGTCTGGGGGCAAGGGACCGTCACCGTCTCCTCAG

.....

.....

—

TTTTCTGGCC TGACAACCAG GGTGGCGCAG GATGCTCAGT GCAGAGAGGA 50

AGAAGCAGGT GGTCTCTGCA GCTGGAAGCT CAGCTCCCAC CCAGCTGCTT 100

TGCATGTCCC TCCCAGCTGC CCTACCTTCC AGAGCCATA TCAATGCCTG 150

TGTCAGAGCC CTGGGGAGGA ACTGCTCAGT TAGGACCCAG AGGGAACCAT 200

GGAAGCCCCA GCTCAGCTTC TCTTCCTCCT GCTACTCTGG CTCCCAGgtg 250
 tGluAlaPro AlaGlnLeuL euPheLeuLe uLeuLeuTrp LeuPro
 agggggaacc atgaggtggt tttgcacatt agtgaaaact cttgccacct 300

ctgctcagca agaaatataa ttaaaattca aagtatatca acaatttttg 350

ctctactcaa agacagttgg tttgatcttg attacatgag tgcatttctg 400

ttttatttcc aatttcagAT ACCACCGGAG AAATTGTGTT GACACAGTCT 450
 Asp ThrThrGlyG luIleValLe uThrGlnSer
 CCAGCCACCC TGTCTTTGTC TCCAGGGGAA AGAGCCACCC TCTCCTGCAG 500
 ProAlaThrL euSerLeuSe rProGlyGlu ArgAlaThrL euSerCysAr
 GGCCAGTCAG AGTGTTAGCA GCTACTTAGC CTGGTACCAA CAGAAACCTG 550
 gAlaSerGln SerValSerS erTyrLeuAl aTrpTyrGln GlnLysProG
 GCCAGGCTCC CAGGCTCCTC ATCTATGATG CATCCAACAG GGCCACTGGC 600
 lyGlnAlaPr oArgLeuLeu IleTyrAspA laSerAsnAr gAlaThrGly
 ATCCCAGCCA GGTTCACTGG CAGTGGGTCT GGGACAGACT TCACTCTCAC 650
 IleProAlaA rgPheSerGl ySerGlySer GlyThrAspP heThrLeuTh
 CATCAGCAGC CTAGAGCCTG AAGATTTTGC AGTTTATTAC TGTCAGCAGC 700
 rIleSerSer LeuGluProG luAspPheAl aValTyrTyr CysGlnGlnA
 GTAGCAACTG GCCTCCCACA GTGATTCCAC ATGAAACAAA AACCCCAACA 750
 rgSerAsnTr pPro
 AGACCATCAG TGTTTACTAG ATTATTATAC CAGCTGCTTC CTTTACAGAC 800

AGCTAGTGGG GT 812

FIG. 41

AGGGCGGCGC AGATGCTCAG TGCAGAGAGA AGAAACAGGT GGTCTCTGCA 50
 GCTGGAAGCT CAGCTCCCAC CCCAGCTGCT TTGCATGTCC CTCCCAGCTG 100
 CCCTACCTTC CAGAGCCCAT ATCAATGCCT GGGTCAGAGC TCTGGGGAGG 150
 AACTGCTCAG TTAGGACCCA GACGGAACCA TGGAAGCCCC AGCGCAGCTT 200
 M etGluAlaPr oAlaGlnLeu
 CTCTTCCTCC TGCTACTCTG GCTCACAGgt gaggggaata tgaggtgtct 250
 LeuPheLeuL euLeuLeuTr pLeuThr
 ttgcacatca gtgaaaactc ctgccacctc tgctcagcaa gaaatataat 300
 taaaattcaa aatagatcaa caatthttggc tctactcaaa gacagtgggt 350
 ttgattttga ttacatgagt gcattttctgt tttattttcca atttcagATA 400
 AspT
 CCACCGGAGA AATTGTGTTG ACACAGTCTC CAGCCACCCT GTCTTTGTCT 450
 hrThrGlyGl uIleValLeu ThrGlnSerP roAlaThrLe uSerLeuSer
 CCAGGGGAAA GAGCCACCCT CTCCTGCAGG GCCAGTCAGG GTGTTAGCAG 500
 ProGlyGluA rgAlaThrLe uSerCysArg AlaSerGlnG lyValSerSe
 CTACTTAGCC TGGTACCAGC AGAAACCTGG CCAGGCTCCC AGGCTCCTCA 550
 rTyrLeuAla TrpTyrGlnG lnLysProGl yGlnAlaPro ArgLeuLeuI
 TCTATGATGC ATCCAACAGG GCCACTGGCA TCCCAGCCAG GTTCAGTGGC 600
 leTyrAspAl aSerAsnArg AlaThrGlyI leProAlaAr gPheSerGly
 AGTGGGCCTG GGACAGACTT CACTCTCACC ATCAGCAGCC TAGAGCCTGA 650
 SerGlyProG lyThrAspPh eThrLeuThr IleSerSerL euGluProGl
 AGATTTTGCA GTTTATTACT GTCAGCAGCG TAGCAACTGG CATCCACAG 700
 uAspPheAla ValTyrTyrC ysGlnGlnAr gSerAsnTrp His
 TGATTCCACA TGAAACAAAA ACCCCAACAA GACCATCAGT GTTTACTAGA 750
 TTATTATACC AGCTGCTTCC TTTACAGACA GCTAGTGGGG TGGCCACTCA 800
 GTGTTAGCAT CTCAGCTCTA TTTGGCCATT TTGGAGTTCA AGTTGTCAAG 850
 TCCAAAATTA CTTATGTTAG TCCATTGCAT CATACCATT T CAGTGTGGCT 900

FIG. 42

CCGCCCCAGC TGCTTTGCAT GTCCCTCCCA GCCGCCCTGC AGTCCAGAGC 50

CCATATCAAT GCCTGGGTCA GAGCTCTGGA GAAGAGCTGC TCAGTTAGGA 100

ACCCCAGAGG GAACCATGGA AACCCCAGCG CAGCTTCTCT TCCTCCTGCT 150
MetGl uThrProAla GlnLeuLeuP heLeuLeuLe

ACTCTGGCTC CCAGgtgagg ggaacatggg atgggttttgc atgtcagtga 200
uLeuTrpLeu Pro

aaaccctctc aagtcctggt acctggcaac tctgctcagt caatacaata 250

attaaagctc aatataaagc aataattctg gctcttctgg gaagacaatg 300

ggtttgattt agattacatg ggtgactttt ctgtttttatt tccaatctca 350

gATACCACCG GAGAAATTGT GTTGACGCAG TCTCCAGGCA CCCTGTCTTT 400
AspThrThrG lyGluIleVa lLeuThrGln SerProGlyT hrLeuSerLe

GTCTCCAGGG GAAAGAGCCA CCCTCTCCTG CAGGGCCAGT CAGAGTGTTA 450
uSerProGly GluArgAlaT hrLeuSerCy sArgAlaSer GlnSerValS

GCAGCAGCTA CTTAGCCTGG TACCAGCAGA AACCTGGCCA GGCTCCCAGG 500
erSerSerTy rLeuAlaTrp TyrGlnGlnL ysProGlyGl nAlaProArg

CTCCTCATCT ATGGTGCATC CAGCAGGGCC ACTGGCATCC CAGACAGGTT 550
LeuLeuIleT yrGlyAlaSe rSerArgAla ThrGlyIleP roAspArgPh

CAGTGGCAGT GGGTCTGGGA CAGACTTCAC TCTCACCATC AGCAGACTGG 600
eSerGlySer GlySerGlyT hrAspPheTh rLeuThrIle SerArgLeuG

AGCCTGAAGA TTTTGCAGTG TATTACTGTC AGCAGTATGG TAGCTCACCT 650
luProGluAs pPheAlaVal TyrTyrCysG lnGlnTyrGl ySerSerPro

CCACAGTGA TTCAGCTTGA AACAAAAACC TCTGCAAGAC CTTCATTGTT 700

TACTAGATTA TACCAGCTGC TTCCTTTACA GATAGCTGCT GCAATGACAA 750

CTCAATTTAG CATCTCTCTC TGCTTGGGCA TTTTGGGGAT CTAAAAAAG 800

TAATCCCTTG ATATATTTTT GACTCTGATT CCTGCATTTT TCCTCAGACC 850

AAGATGGACA GCCAGGTTTA AGCACAGTTT CACAGTAATG GCCACTGGAT 900

FIG. 43

AAACACATTC TCTGCAGACA AATTTGAGCT ACCTTGATCT TACCTGGACA 50

GGTGGGGACA CTGAGCTGGT GCTGAGTTAC TCAGATGCGC CAGCTCTGCA 100

GCTGTGCCCCA GCCTGCCCCA TCCCCTGCTC ATTTGCATGT TCCCAGAGCA 150

CAACCTCCTG CCCTGAAGCC TTATTAATAG GCTGGTCAGA CTTTGTGCAG 200

GAATCAGACC CAGTCAGGAC ACAGCATGGA CATGAGGGTC CTCGCTCAGC 250
MetAs pMetArgVal LeuAlaGlnL

TCCTGGGGCT CCTGCTGCTC TGTTTCCAG gtaaggatgg agaacactag 300
euLeuGlyLe uLeuLeuLeu CysPhePro

cagtttactc agcccagggt gctcagtact gctttactat tcagggaaat 350

tctcttacia catgattaat tgtgtggaca tttgttttta tgtttccaat 400

ctcagGTGCC AGATGTGACA TCCAGATGAC CCAGTCTCCA TCCTCACTGT 450
GlyAla ArgCysAspI leGlnMetTh rGlnSerPro SerSerLeuS

CTGCATCTGT AGGAGACAGA GTCACCATCA CTTGTGCGGC GAGTCAGGGT 500
erAlaSerVa lGlyAspArg ValThrIleT hrCysArgAl aSerGlnGly

ATTAGCAGCT GGTTAGCCTG GTATCAGCAG AAACCAGAGA AAGCCCCTAA 550
IleSerSerT rpLeuAlaTr pTyrGlnGln LysProGluL ysAlaProLy

GTCCTGATC TATGCTGCAT CCAGTTTGCA AAGTGGGGTC CCATCAAGGT 600
sSerLeuIle TyrAlaAlaS erSerLeuGl nSerGlyVal ProSerArgP

TCAGCGGCAG TGGATCTGGG ACAGATTTCa CTCTCACCAT CAGCAGCCTG 650
heSerGlySe rGlySerGly ThrAspPheT hrLeuThrIL eSerSerLeu

CAGCCTGAAG ATTTTGCAAC TTATTACTGC CAACAGTATA ATAGTTACCC 700
GlnProGluA spPheAlaTh rTyrTyrCys GlnGlnTyrA snSerTyrPr

ACCCACAGTG TTACACACCC AAACATAAAC CCCCAGGGAA GCAGATGTGT 750
o

GAGGCTGGGC TGCCCCAGCT GCTTCTCCTG ATGCCTCCAT CAGCTGAGAG 800

TGTTCTCAG ATGCAGCCAC ACTCTGATGG TGTTGGTAGA TGGGGAC 847

FIG. 44

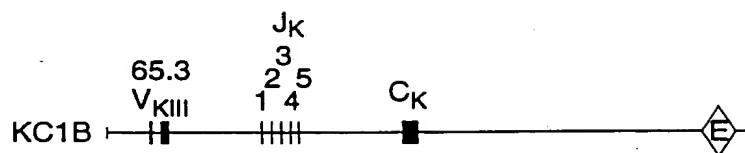
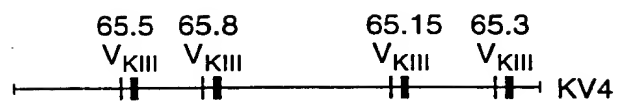


FIG. 45

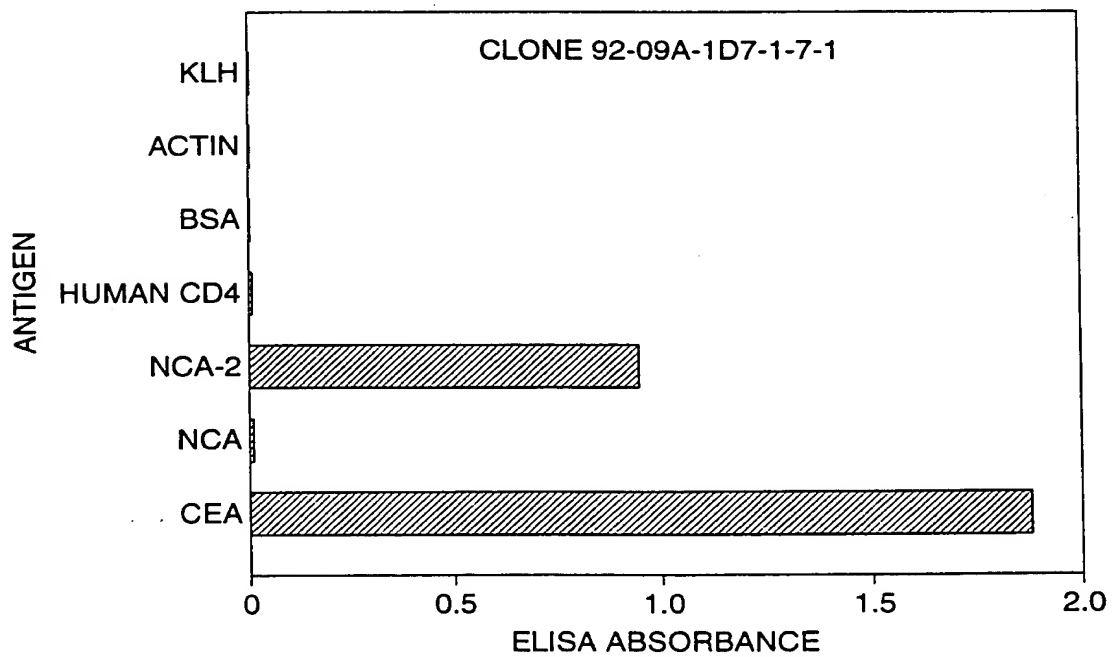
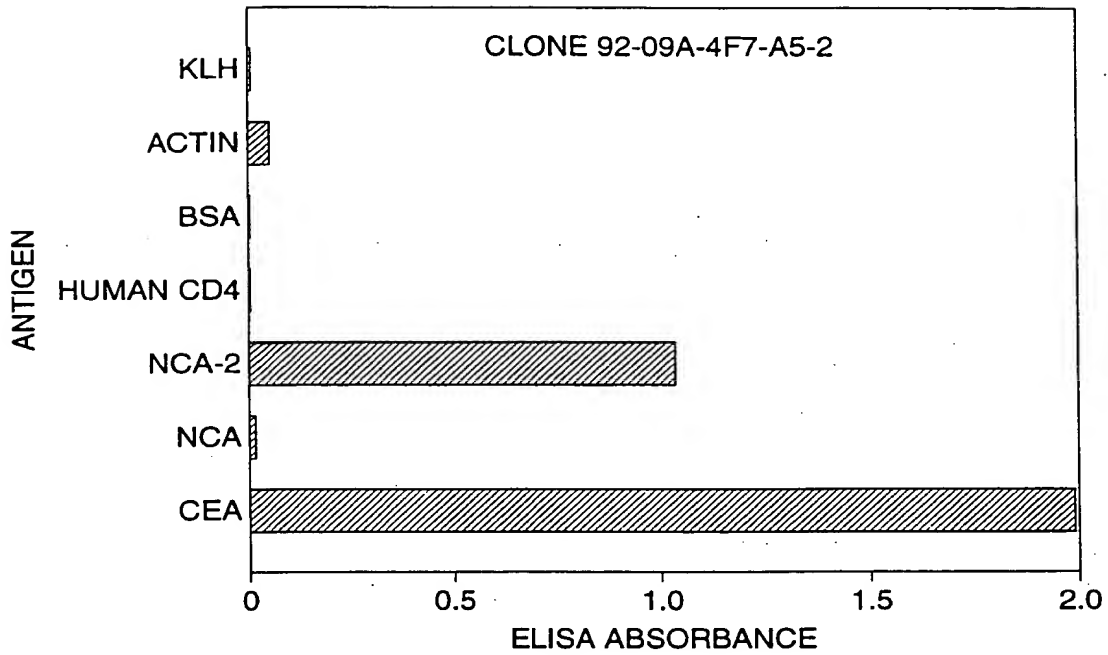


FIG. 46

		VH251	HUMAN n D n		MOUSE Cy
5	DXP'1 J6 G1	GCCTCGACACCGCCATGATGATTACTGTGTGAGA	catttATGGTTCGGGAGTTAcg	CGGtgTGAAGTCTGGGGCCAAGGGACACGGGTCAACGGTCTCTCTCAG	CCAAACGACACACCCCATCTGTCTATCCACT
7	DHQ52' J3 G1	GCCTCGACACCGCCATGATGATTACTGTGTGAGA	cACTGGGcatttagat	GCTcTTGATgTCTGGGGCCAAGGGACAATGcTACCgTCTCTTCAG	CCAAACGACACACCCCATCTGTCTATCCACT
2	DHQ52 J3 G2b	GCCTCGACACCGCCATGATGATTACTGTGTGAGA	ACTGGGcAtgat	GCTTTTGATATCTGGGGCCAAGGGACAATGGTCAcCGTCTCTTCAG	CCAAACGACACACCCCATCTGTCTATCCACT
3	D7 J3 G2b	GaCTCGACACCGCCATGATGATTACTGTGTGAGA	cagggggagagat	GCTTTAGATATCTGGGGCCAAGGGACAATGGTCAcCGTCTCTTCAG	CCAAACGACACACCCCATCTGTCTATCCACT
4	DXP'1 J4 G2b	GCCTCGACACCGCCATGATGATTACTGTGTGAGA	catagggACTATatTTcGGGAGTTATtTcc	TGACTACTGGGGCCAAGGGAACTCTGGTCAcCGTCTCTTCAG	CCAAACGACACACCCCATCTGTCTATCCACT
10	DHQ52 J3 G2b	GCCTCGACACCGCCATGATGATTACTGTGTGAGA	ACTGGGcAtgat	GCTTTTGATATCTGGGGCCAAGGGACAATGGTCAcCGTCTCTTCAG	CCAAACGACACACCCCATCTGTCTATCCACT
1	D7 J3 G3	GCCTCGACACCGCCATGATGATTACTGTGTGAGA	cataggtctatg	GATATCTGGGGCCAAGGGACAATGGTCAcCGTCTCTTCAG	CTACAACACAGCCCCCATCTGTCTATCCCTT
6	DHQ52 J4 G3	GCCTCGACACCGCCATGATGATTACTGTGTGAGA	gagggcggtcAtTGGGcAtcg	TTTGACTATCTGGGGCCAAGGGAACTCTGGTCAcCGTCTCTTCAG	CTACAACACAGCCCCCATCTGTCTATCCCTT
8	DIR2 J3 G3	GCCTCGACACCGCCATGATGATTACTGTGTGAGA	agggACCCCCcttgat	GCTTTTGATATCTGGGGCCAAGGGACAATGGTCAcCGTCTCTTCAG	CTACAACACAGCCCCCATCTGTCTATCCCTT
9	DIR2c J6 G3	GCCTCGACACCGCCATGATGATTACTGTGTGAGA	cgGGGGcCT	TACTACTACTACGGTATGGAGTCTGGGGCCAAGGGACACGGGTCAcCGTCTCTTCAG	CTACAACACAGCCCCCATCTGTCTATCCCTT

FIG. 47

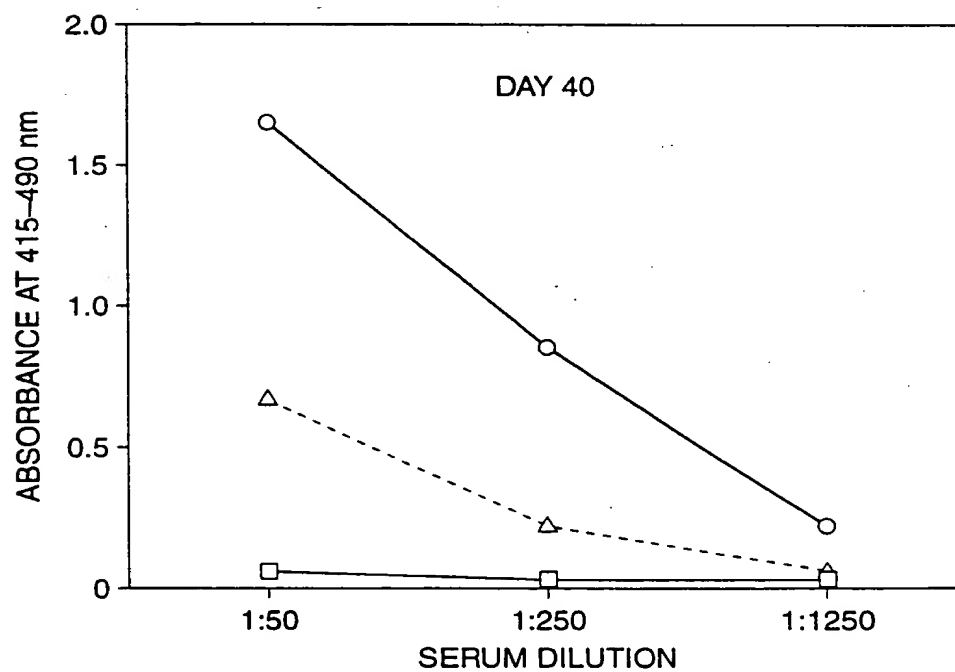
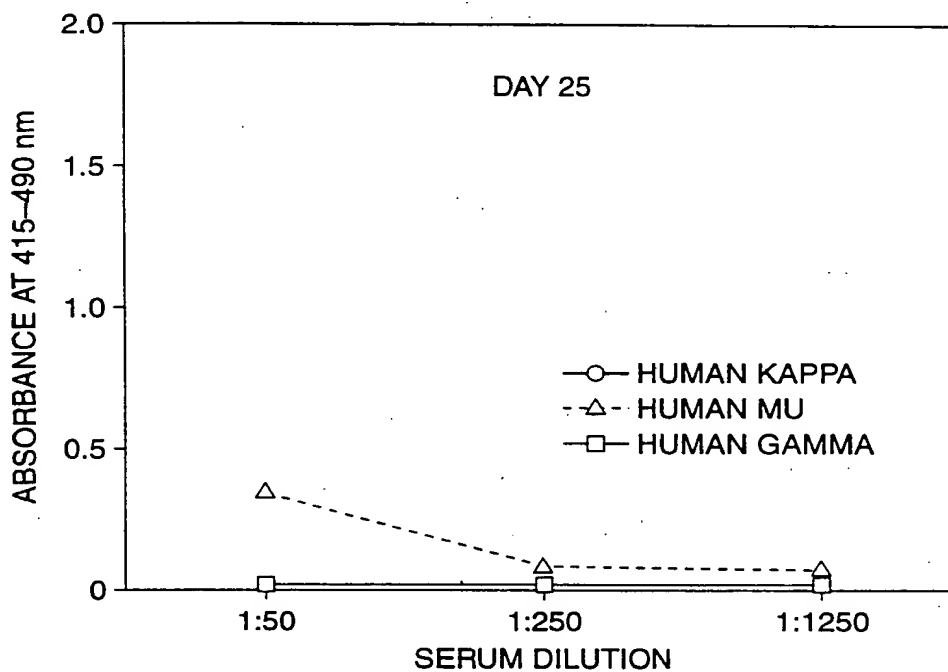


FIG. 48

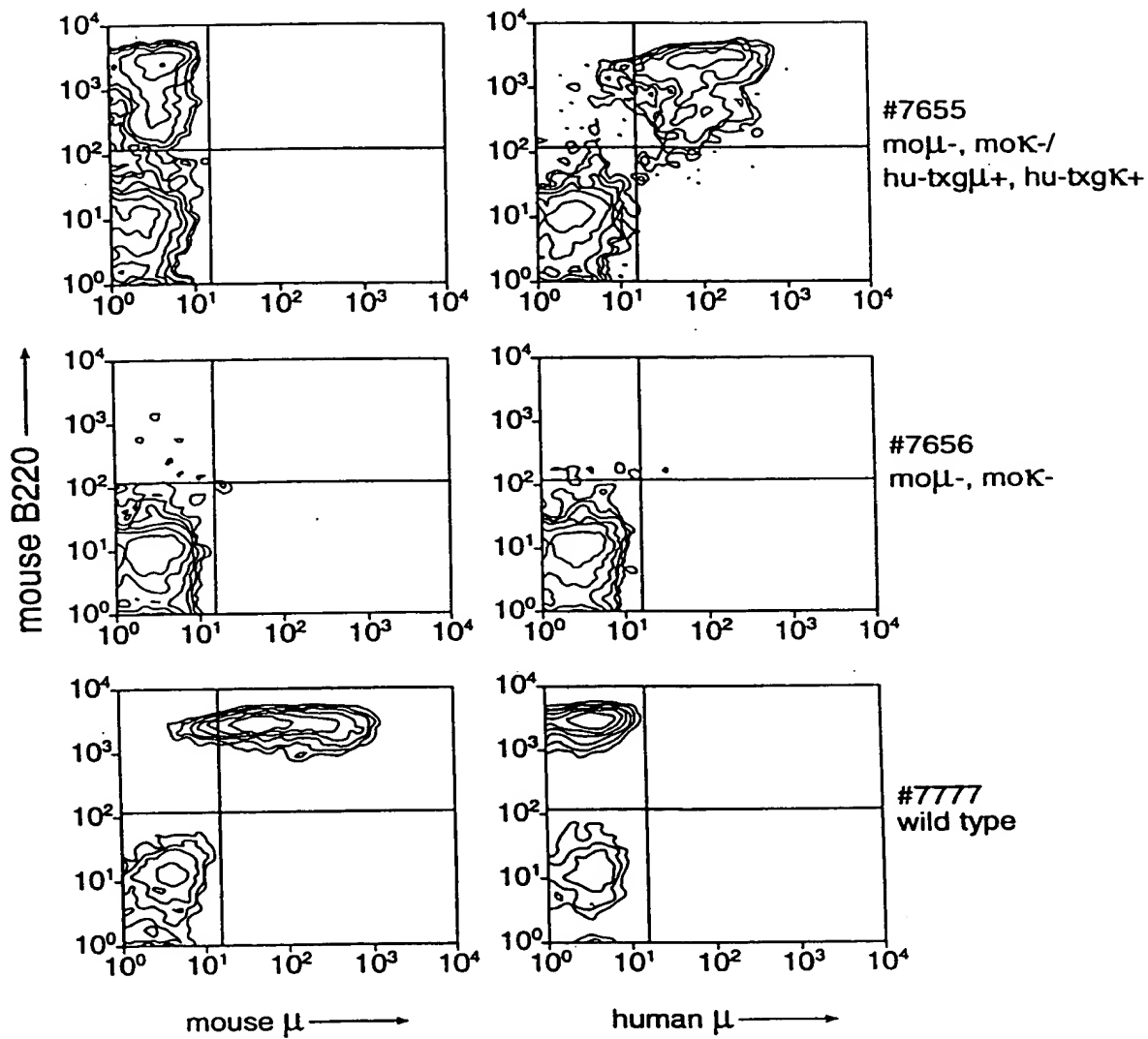


FIG. 49



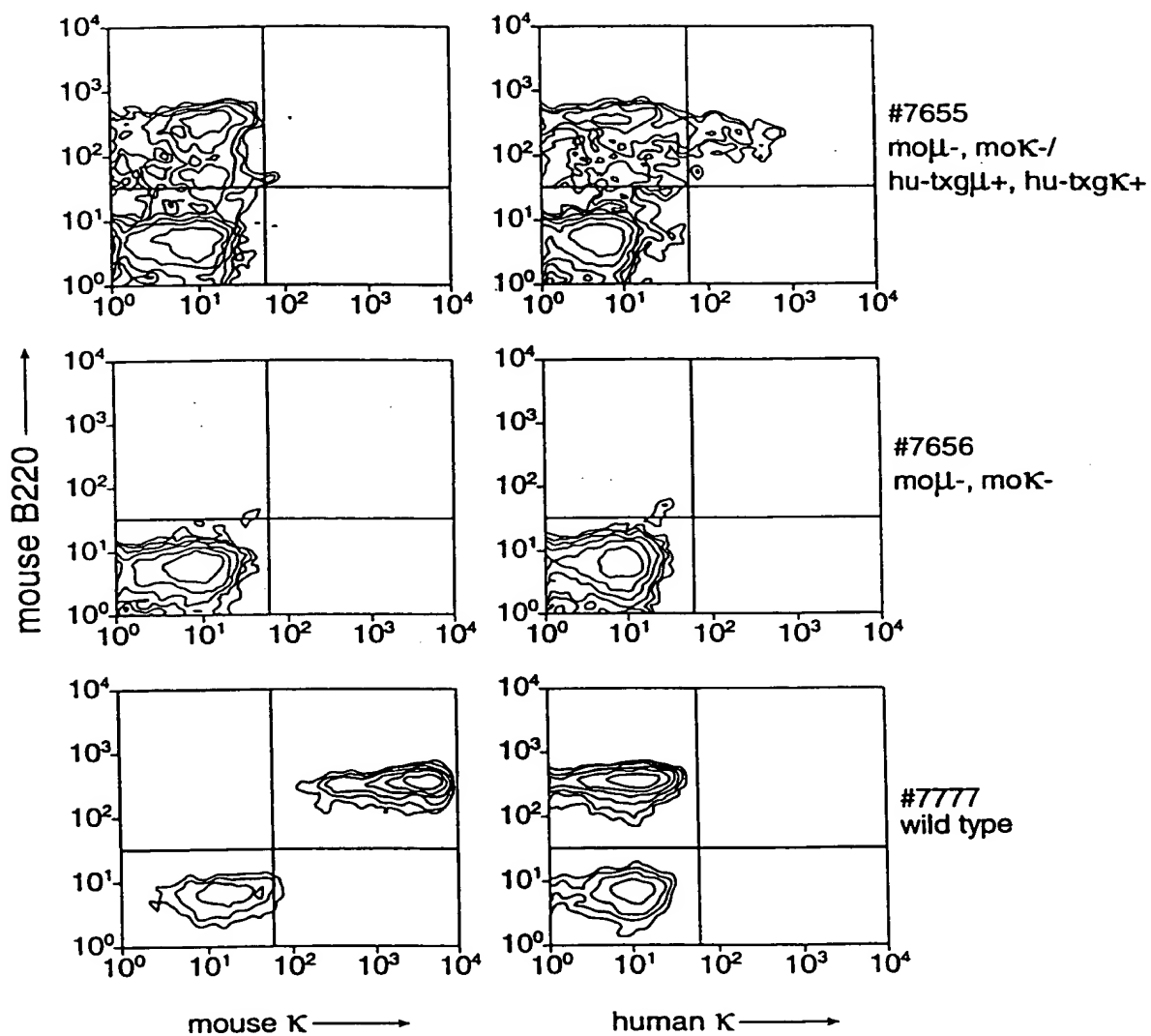
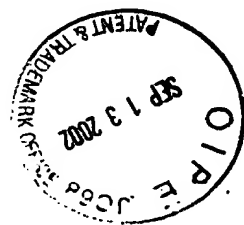


FIG. 50



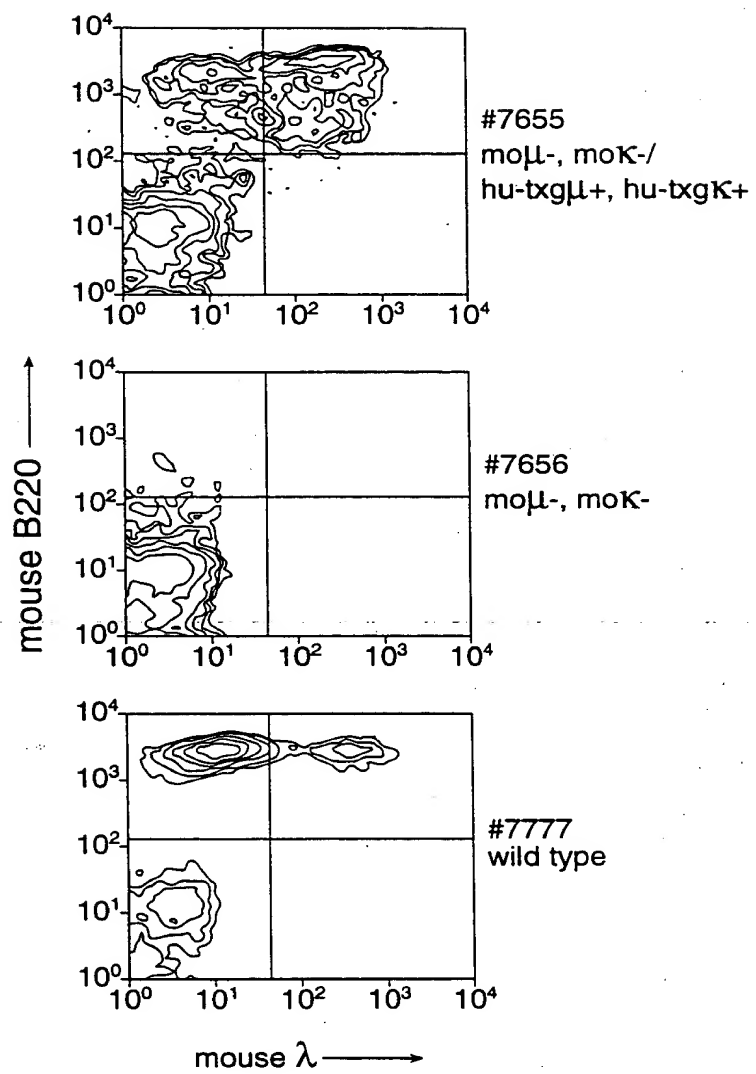


FIG. 51

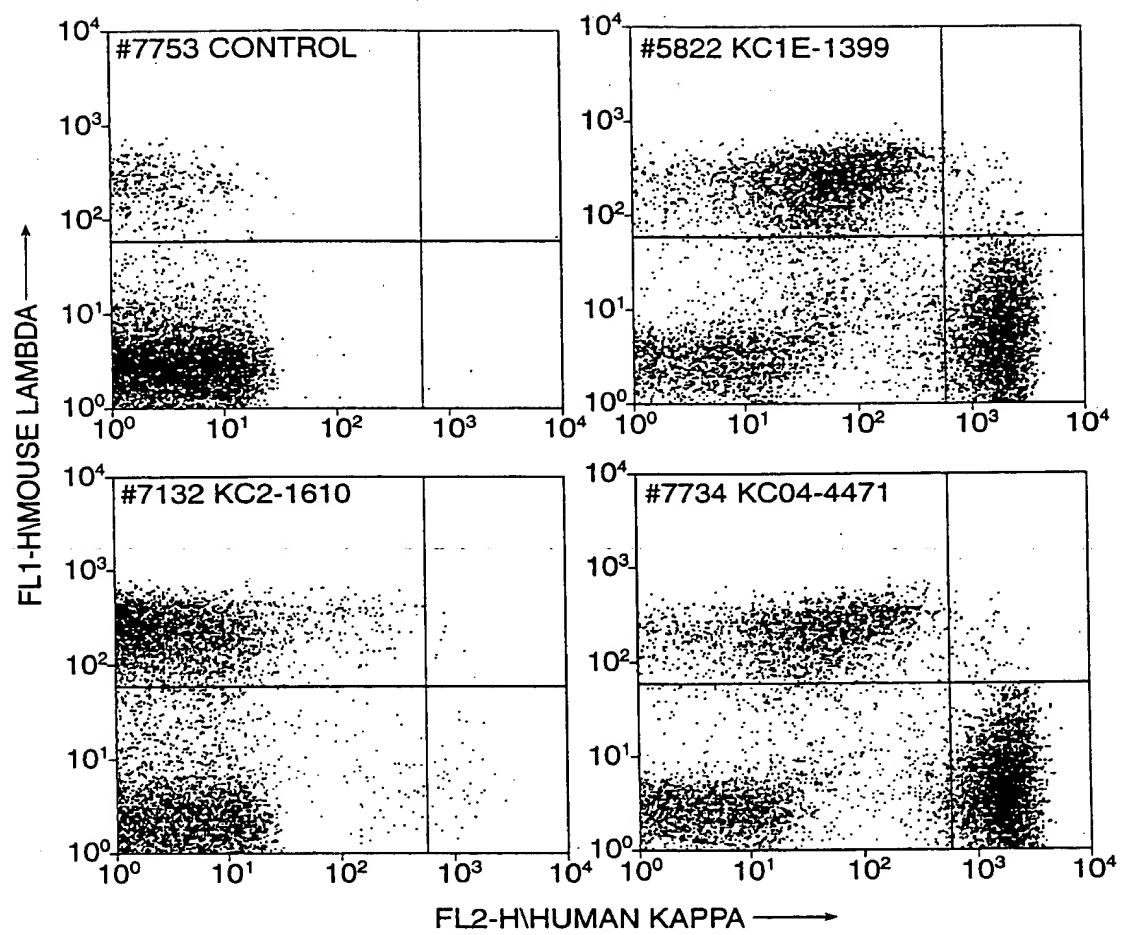


FIG. 52

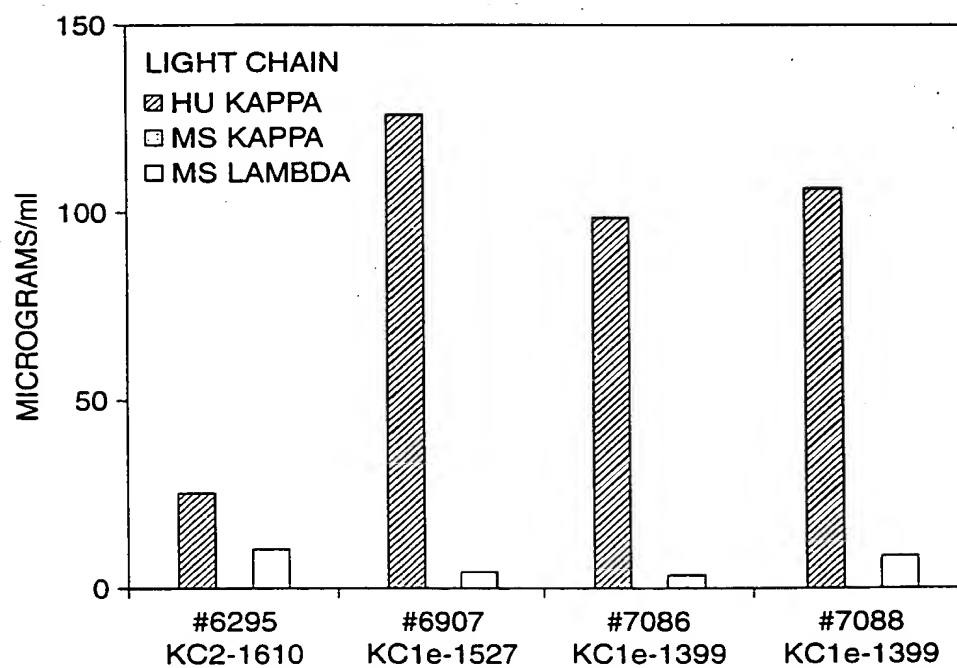
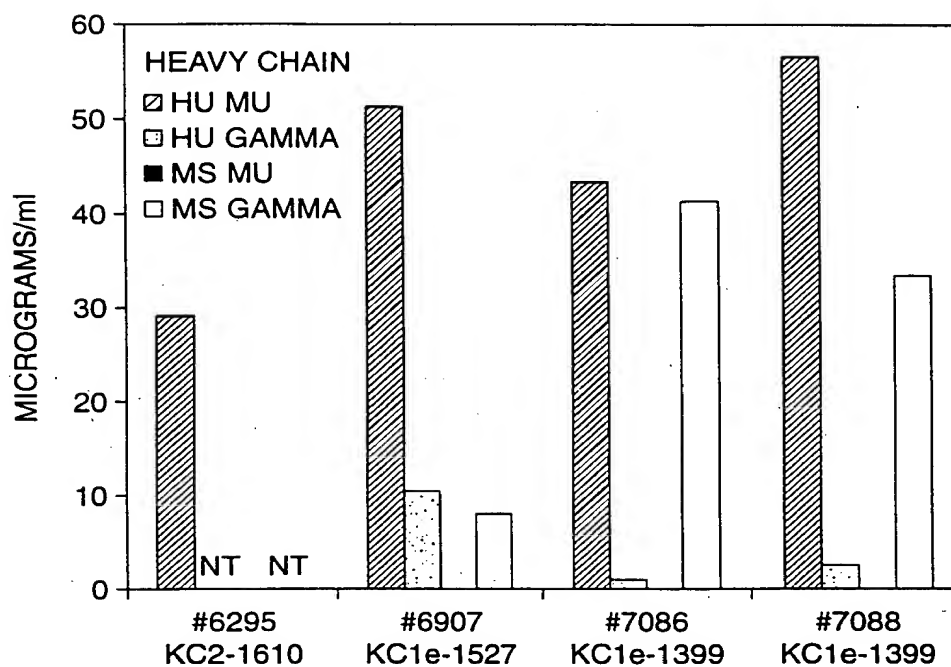


FIG. 53

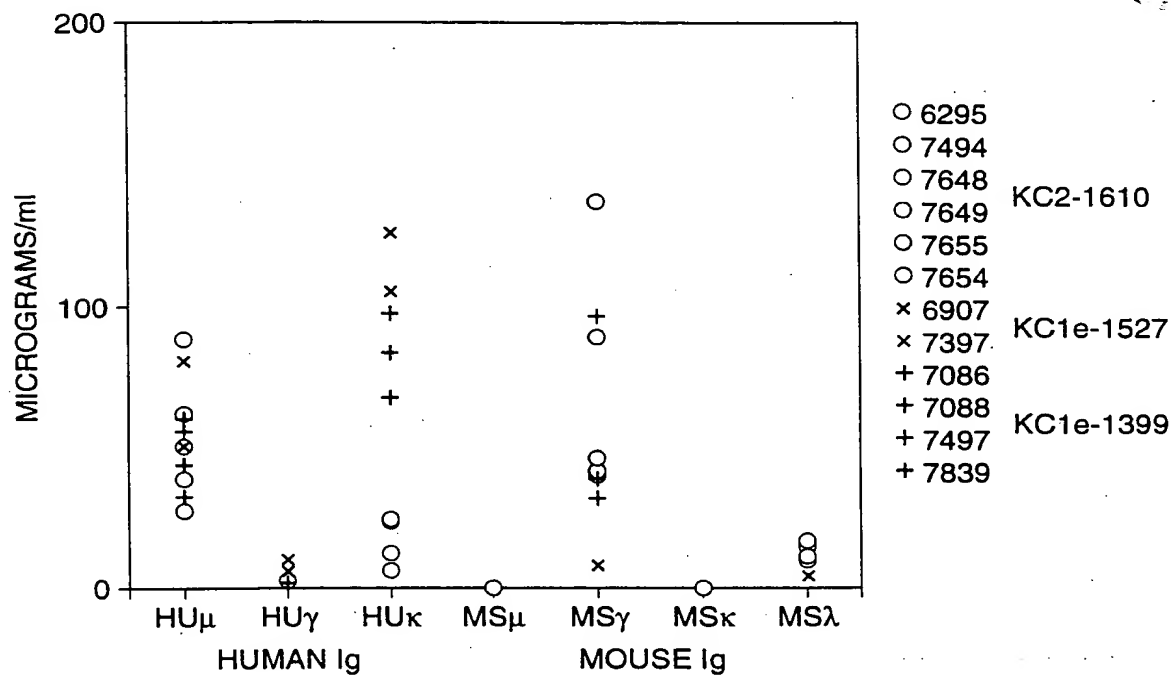


FIG. 54



Anti-human CD4 titers in 0011 mouse

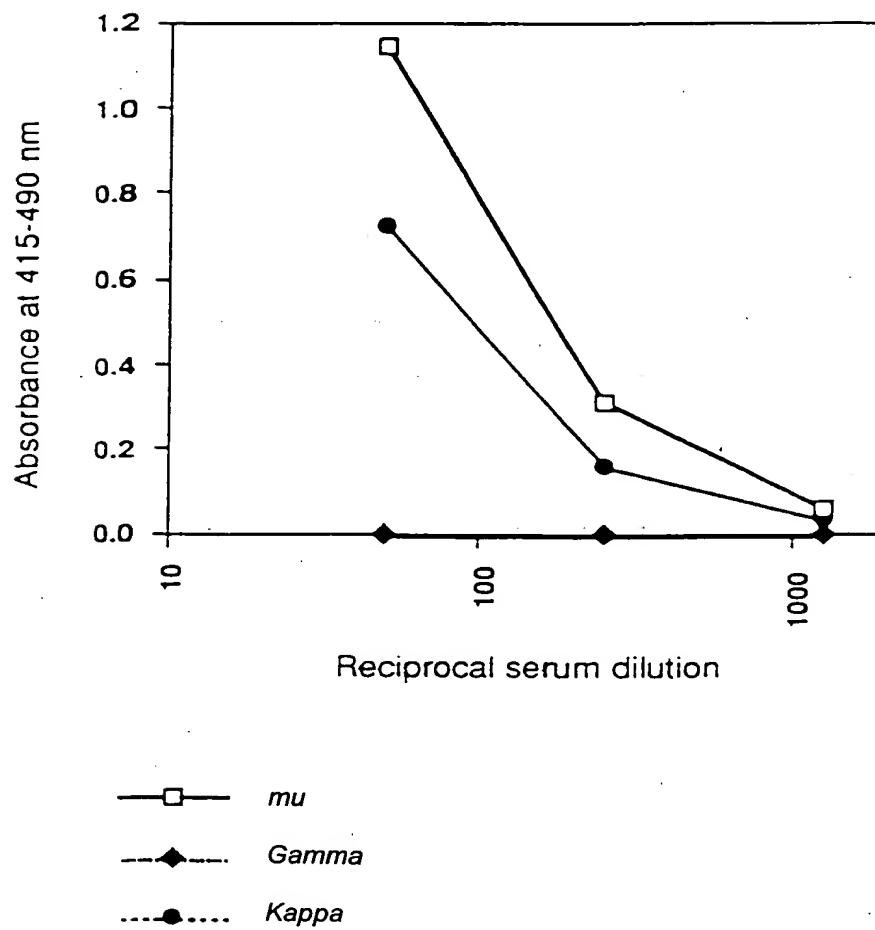


FIGURE 55

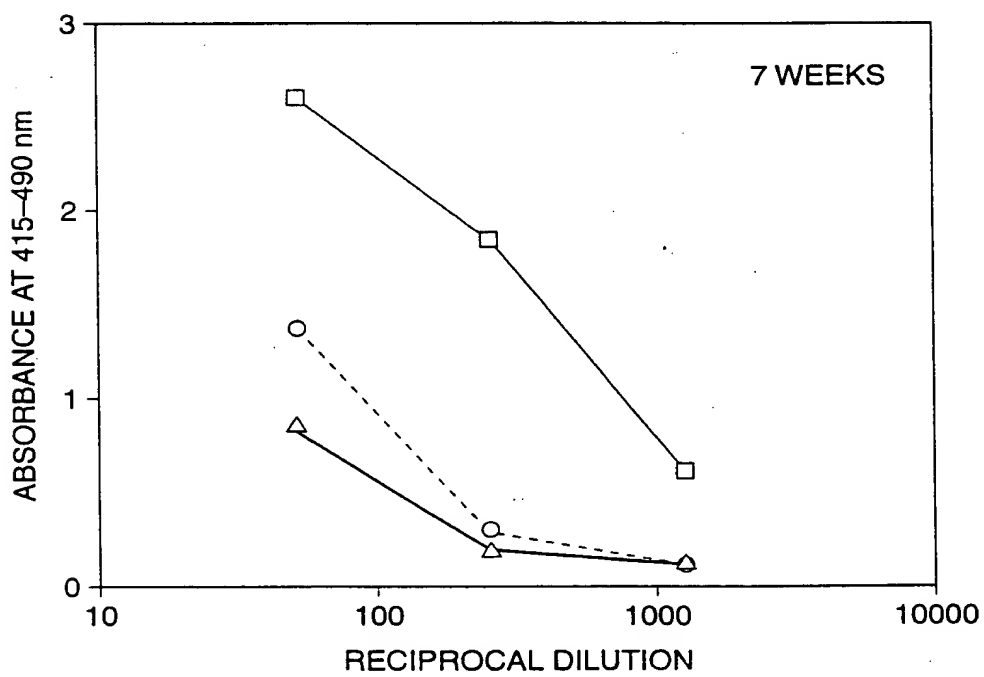
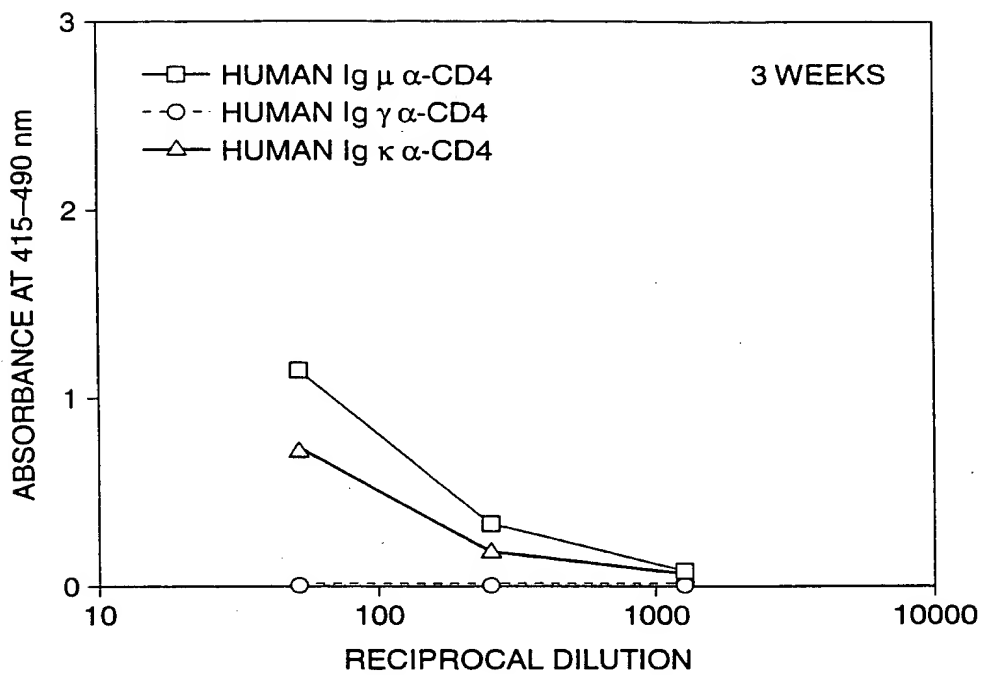


FIG. 56

0 5 10 15 20 25 30 35 40 45Kb

LIGHT CHAIN MINILOC

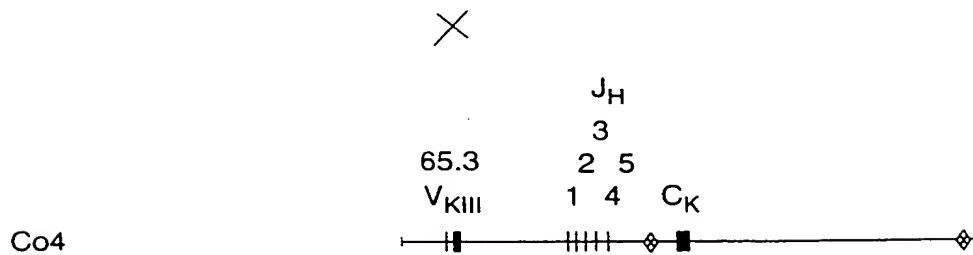
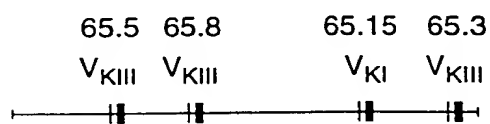
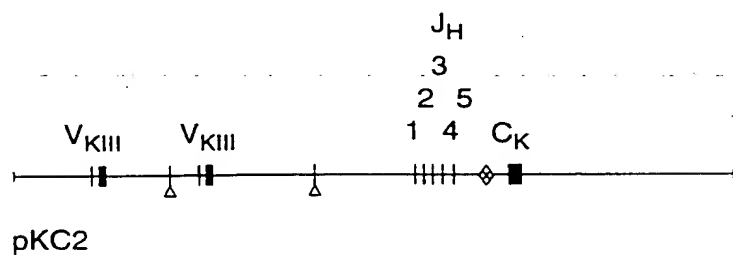
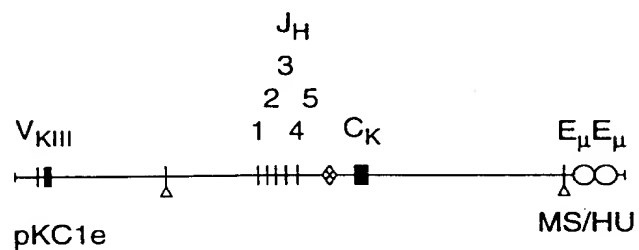
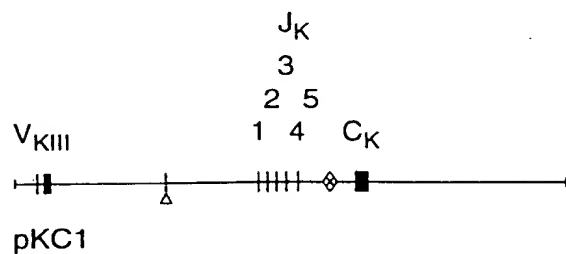
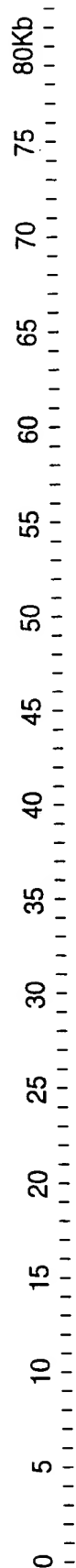


FIG. 57A



HEAVY CHAIN MINILOC

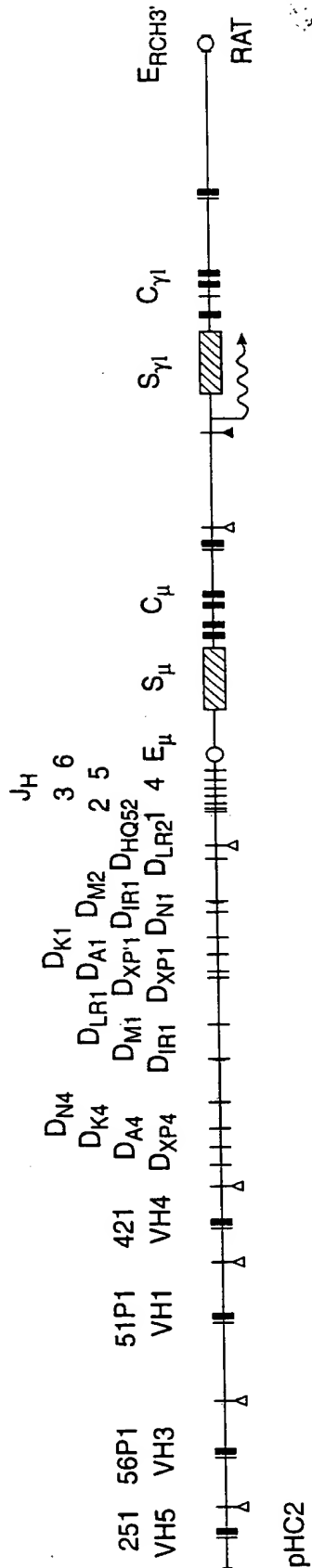
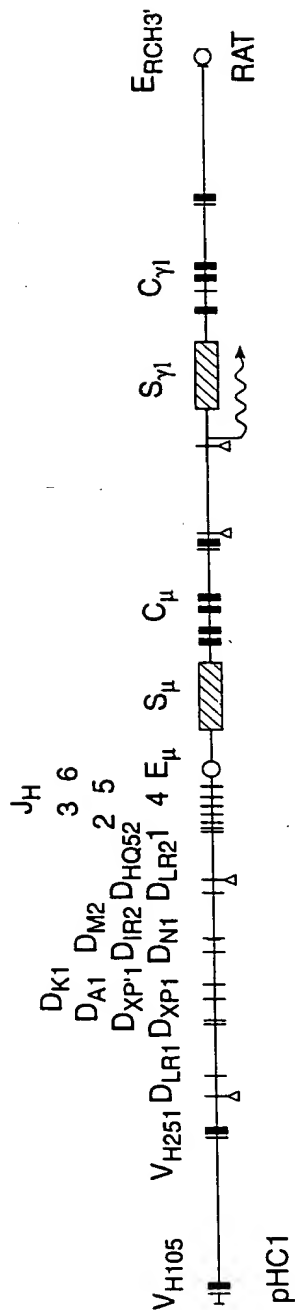


FIG. 57B

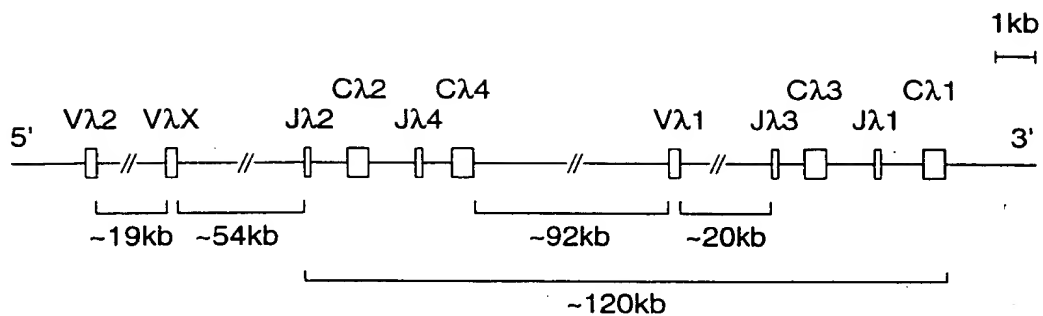
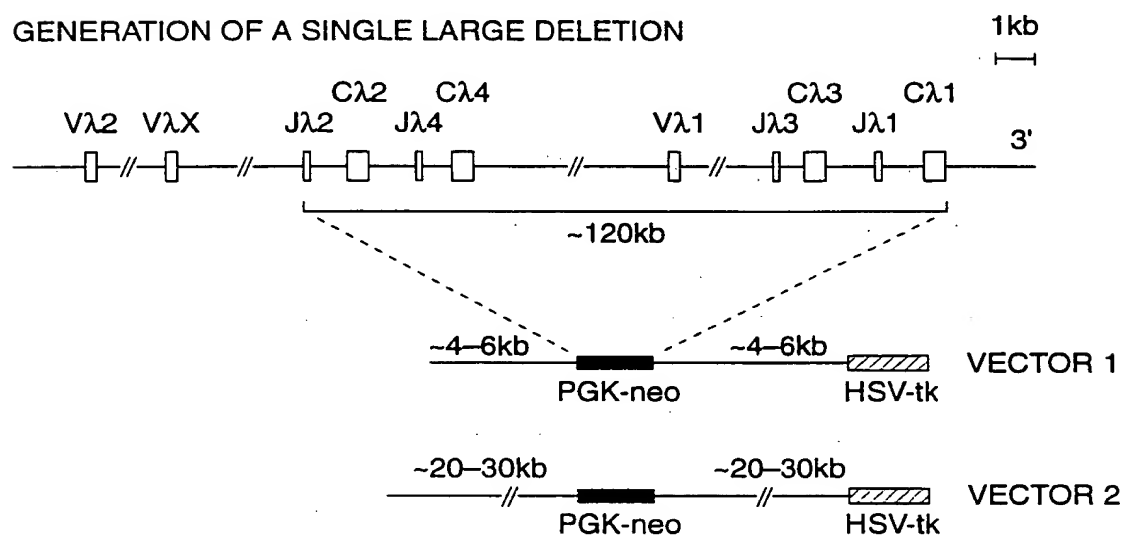


FIG. 58

GENERATION OF A SINGLE LARGE DELETION



GENERATION OF TWO SMALL DELETIONS

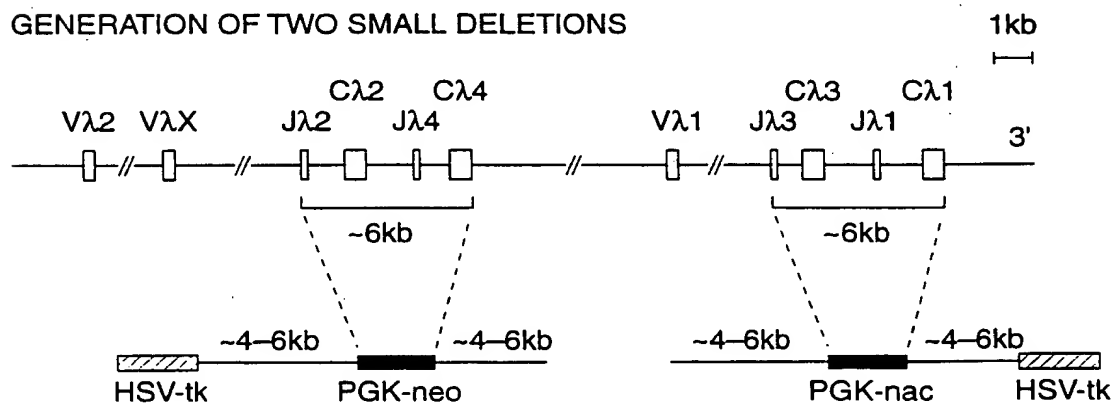


FIG. 59

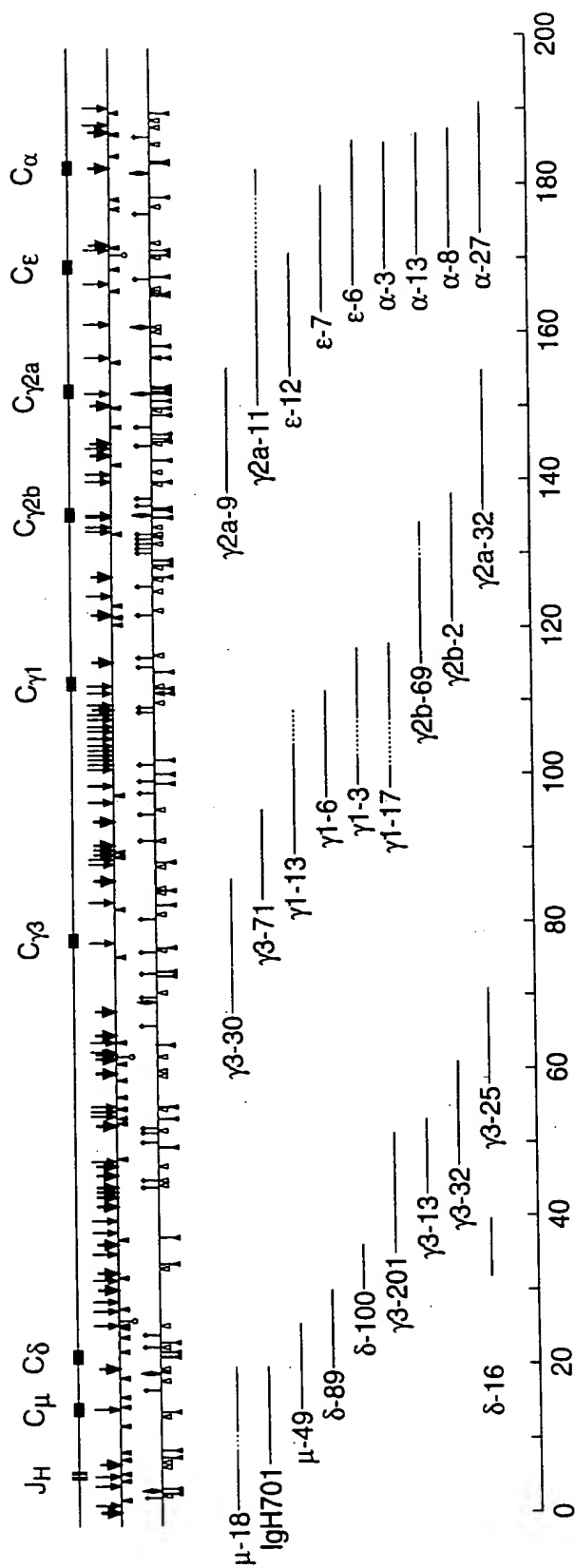


FIG. 60

CGAGAGGGGCGGGGGAAGACTACTATCCCAGGCAGGTTTTAGGTTCCAGAGTCTGCGAG
AAATCCCACCATCTACCCACTGACACTCCCACCAGTCCTGTGCAGTGATCCCGTGATAAT
CGGCTGCCTGATTCACGATTACTTCCCTTTCGGCACGATGAATGTGACCTGGGGAAAGAG
TGGAAGGATATAACCACCGTGAACCTTCCACCTGCCCTCGCCTCTGGGGGACGGTACAC
CATGAGCAGCCAGTTAACCTGCCAGCTGTCGAGTGCCCGAGAAGGAGAGTCCGTGAAATG
TTCCGTGCAACATGACTCTAACCCCGTCCAAGAATTGGATGTGAATTGCTCTGGTAAAGA
ACGTTAGGGGGTTCAGCTAGGGGTGGGATAAGTCCTACCTTATCTAGATCCATATATCCCT
CTGATGCACACCCTCACAGGAATCCCTCAGAAACCTCCACTATGGGGATTGGGGGAAGGA
AGCGTAAACAGGTCTAGAAGGAGCTGGAGGCCTCAGAACATCCAGAAACGGGGACAGCAA
AGGAGACAAGGAGAATATACTGATTTGCTAGGACATCTTCTGTTACAGGTCCTACTCCTC
CTCCTCCTATTACTATTCTTCTGCCAGCCCAGCCTGTCACTGCAGCGGCCAGCTCTTG
AGGACCTGCTCCTGGGTTTCAGATGCCAGCATCACATGTACTCTGAATGGCCTGAGAAATC
CTGAGGGAGCTGCTTTCACCTGGGAGCCCTCCACTGGGAAGGATGCAGTGAGAAGAAAG
CTGCGCAGAATTCTGCGGCTGCTACAGTGTGTCCAGCGTCCTGCCTGGCTGTGCTGAGC
GCTGGAACAGTGGCGCATCATTCAAGTGACAGTTACCCATCCTGAGTCTGGCACCTTAA
CTGGCACAATTGCCAAAGTCACAGGTGAGCTCAGATGCATACCAGGACATTGTATGACGT
TCCCTGCTCACATGCCTGCTTCTTCTCTATAATACAGATGCTCAACTAACTGCTCATGTC
CTTATATCACAGAGGGAAATTGGAGCTATCTGAGGAACTGCCCAGAAGGGAAGGGCAGAG
GGGTCTTGCTCTCCTTGTCTGAGCCATAACTCTTCTTCTACCTTCCAGTGAACACCTTC
CCACCCAGGTCCACCTGCTACCGCCGCCGTGCGAGGAGCTGGCCCTGAATGAGCTCTTG
TCCCTGACATGCCTGGTGCGAGCTTTCAACCCTAAAGAAGTGCTGGTGCGATGGCTGCAT
GGAAATGAGGAGCTGTCCCAGAAAGCTACCTAGTGTTTGAGCCCCTAAAGGAGCCAGGC
GAGGGAGCCACCACCTACCTGGTGACAAGCGTGTTGCGTGTATCAGCTGAAACCTGGAAA
CAGGGTGACCAGTACTCCTGCATGGTGGGCCACGAGGCCTTGCCCATGAACTTCACCCAG
AAGACCATCGACCGTCTGTCGGGTAAACCCACCAATGTCAGCGTGTCTGTGATCATGTCA
GAGGGAGATGGCATCTGCTACTGAGCCACCCTGCCTGTCCCTACTCCTAGAATAAACTCT
GTGCTCATCCAAAGTATCCCTGCACTTCCACCCAGTGCCTGTCCACCACCCTGGGGTCTA
CGAAACACAGGGAGGGGTCAGGGCCCAGGGAGGGAGAAATACCACCACCTAAGC

FIG. 61

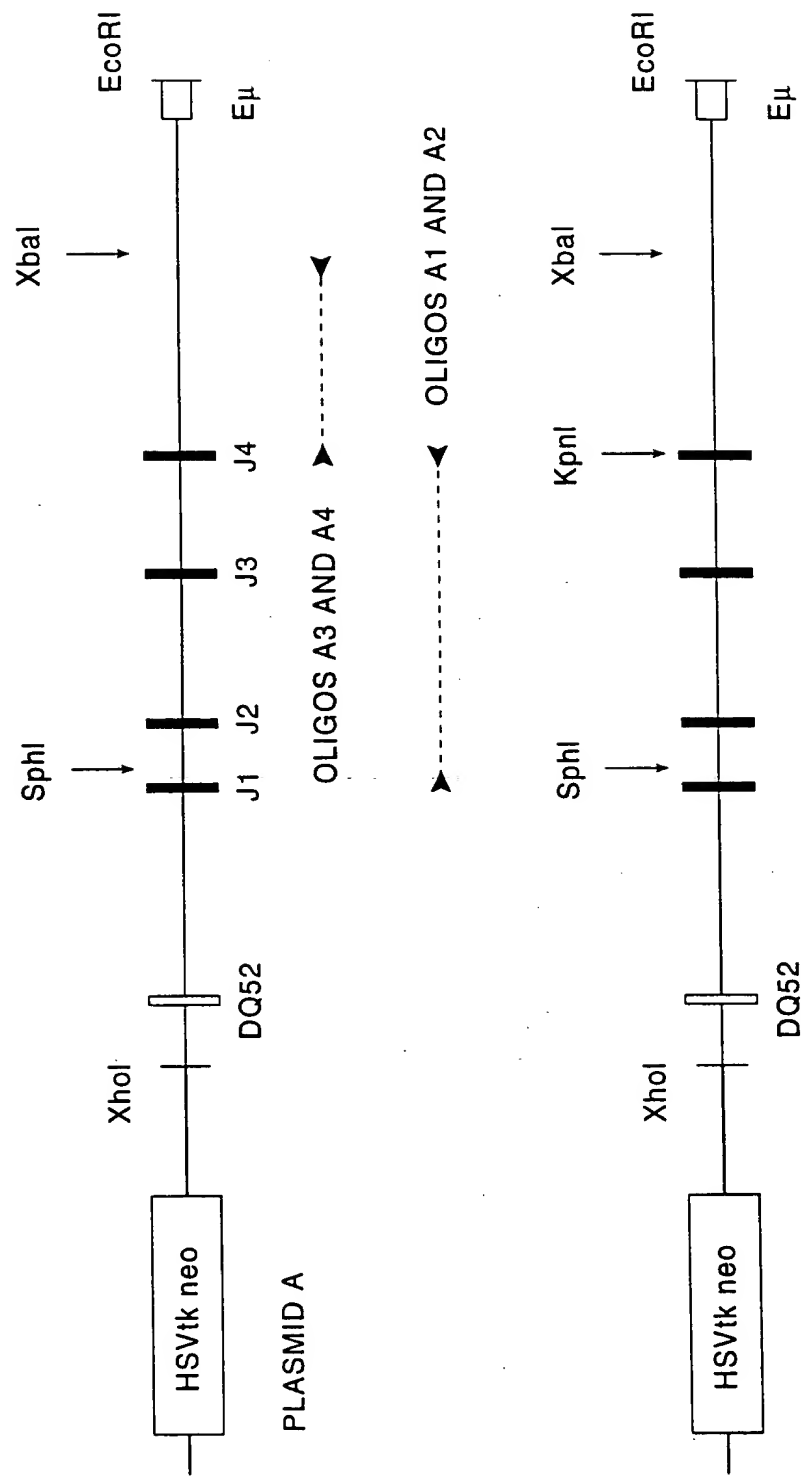


FIG. 62

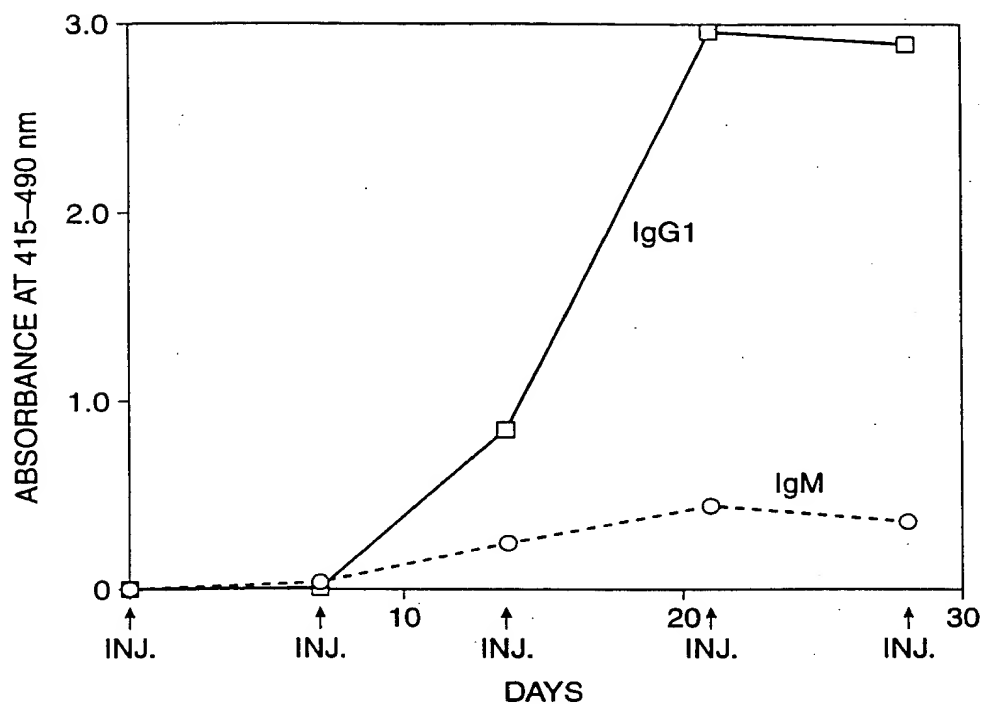


FIG. 63

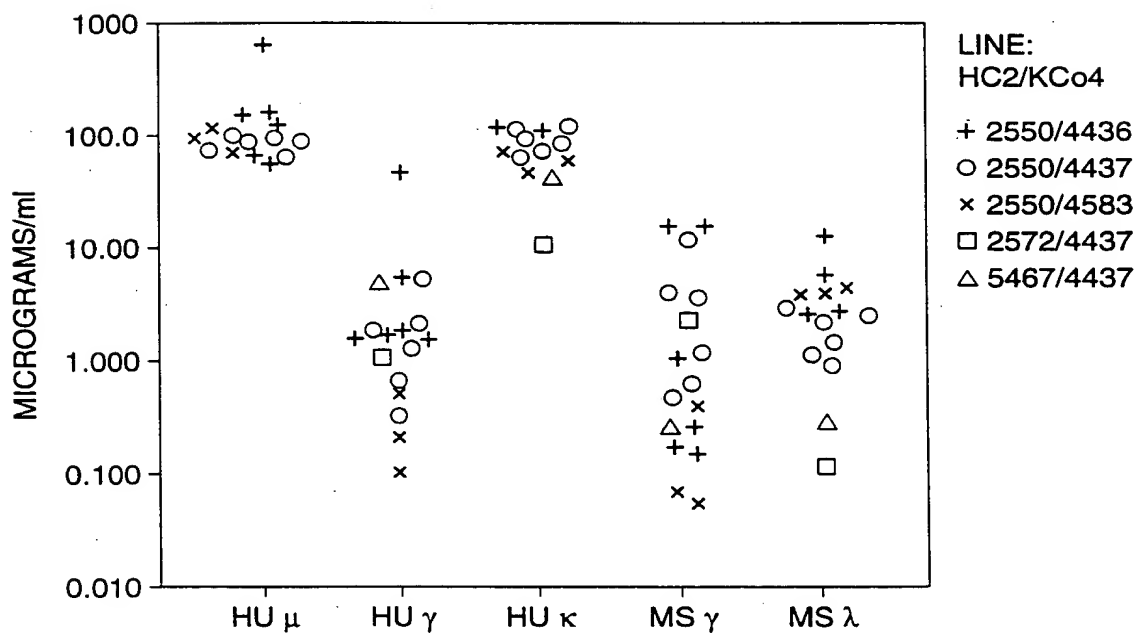


FIG. 70

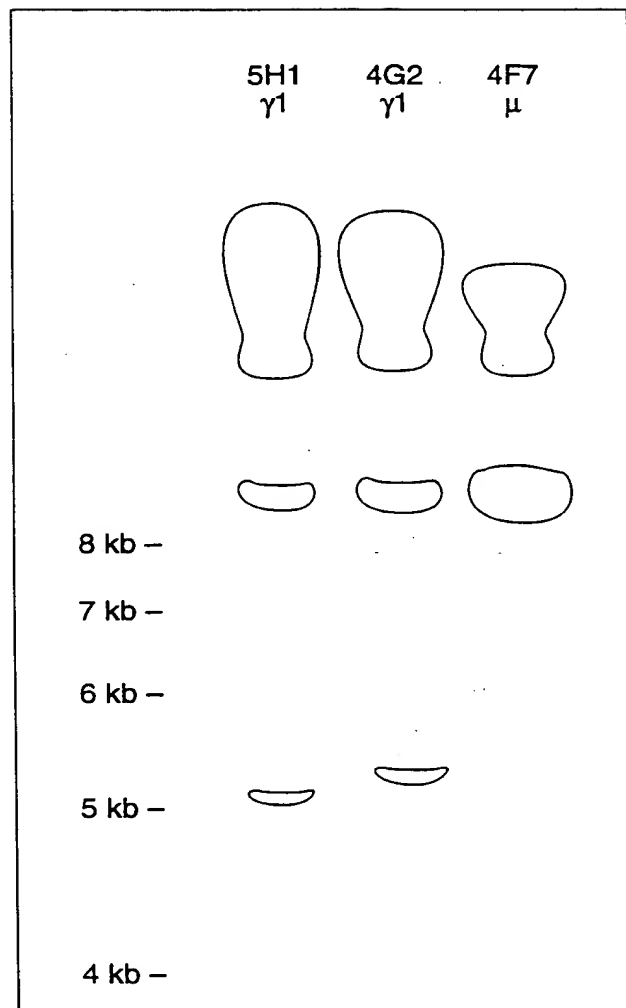


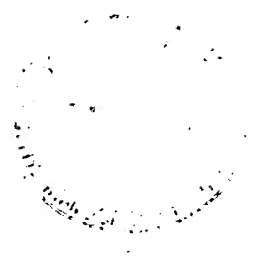
FIG. 64A

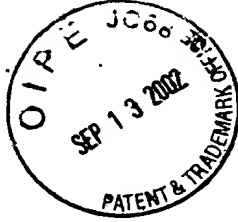


FIG. 64B

VH251	N D N	J	Cγ	mouse γ1
2357.t5 DXP'1 J6 gcctcggaaccgccatgtattactgtgtaga CATTtatggttcggggggttaCG			cggTgtgAacgtctggggccaagggaaccacgggtcaccgctctctctcag ccaaaacgaacaccccccatctgtctatccac	
2357.t7 DH052 J3 gcctcggaaccgccatgtattactgtgtaga CactgggCATTGGAT			gctCttgatGtctggggccaagggaacantgGtaaccgtctctctcag ccaaaacgaacaccccccatctgtctatccac	mouse γ2b
2357.t2 DH052 J3 gcctcggaaccgccatgtattactgtgtaga actgggggATGAT			gctttttgatattctggggccaagggaacantgggtcaccgctctctctcag ccaaaacgaacaccccccatctgtctatccac	
2357.t3 D? J3 gactcggaaccgccatgtattactgtgtaga CAGGGGAGAGAT			gcttttagattctggggccaagggaacantgggtcaccgctctctctcag ccaaaacgaacaccccccatctgtctatccac	
2357.t4 DXP'1 J4 gcctcggaaccgccatgtattactgtgtaga CATAGGgactataTtcgggggagtattTTCC			tgactactggggccaagggaacccctgggtcaccgctctctctcag ccaaaacgaacaccccccatctgtctatccac	
2357.t10 DH052 J3 gcctcggaaccgccatgtattactgtgtaga actgggggATGAT			gctttttgatattctggggccaagggaacantgggtcaccgctctctctcag ccaaaacgaacaccccccatctgtctatccac	mouse γ3
2357.t1 D? J3 gcctcggaaccgccatgtattactgtgtaga CATGGGTCTATG			gatattctggggccaagggaacantgggtcaccgctctctctcag ctacaacgaacagcccccatctgtctatccct	
2357.t6 DH052 J4 gcctcggaaccgccatgtattactgtgtaga GAGAGCGGTcactgggggATCG			tttgactaTtggggccaagggaacccctgggtcaccgctctctctcag ctacaacgaacagcccccatctgtctatccct	
2357.t8 DIR2 J3 gcctcggaaccgccatgtattactgtgtaga AGGgacccccCTGAT			gctttttgatattctggggccaagggaacantgggtcaccgctctctctcag ctacaacgaacagcccccatctgtctatccct	
2357.t9 DIR2R J6 gcctcggaaccgccatgtattactgtgtaga CGggggcct			tactactactacgtatggacgtctggggccaagggaacacgggtcaccgctctctctcag ctacaacgaacagcccccatctgtctatccct	mouse

FIG. 65

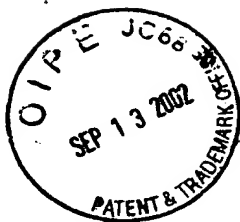




20 30 40 50 52 a 53 60
VH251.6L TCTCTGAAGATCTCTGTAAAGGTTCTGGATACAGCTTTACCACTACTGGATCGGCTGGGTGGCCAGATGCCCCGGGAAGGCCCTGGAGTGGATGGGGATCATCTATCTGGTGACTCTGTATACCAAGATACAGCCCGTCTTCCAAAGGCCAGGTC
J2
2599.7
2599.9
2599.11
2599.14
J3
2599.25
J4
2599.2
2599.5
2599.8
2599.23
2599.24
2599.28
J6
2599.10
2599.13

_____ COR I
_____ COR II

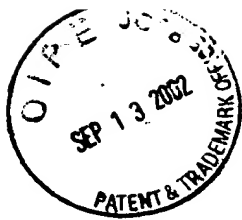
FIG. 66A-1



70	80	82 a b c 83	90
ACCATCTCAGCCGACAAAGTCCATCAGACCGGCTACTCTGAGTGGAGCAGCTCGAGGCTCGGACACCCCATGTATTACTGTCCGAGA			
.....	CAAGGactgggaag		DHQ52
.....	CAGAAAGGGGGAAGG	
.....	CAGAAAGGGGGAAGG		DHQ52
.....	actgggtgg	
.....	CATGaaactgggaTCCGGG		DHQ52
.....	ACGgattacgatattttgactggttattataacCT		DXP1
.....	tatagcagcCTT		DN1
.....	TCTtactatggttcggggg		DXP'1
.....	CTCGattacgatattttgactggttattataacCC		DXP1
.....	CTCGattacgatattttgactggttattataacCC		DXP1
.....	CCGtatagcagcgtgtacAGG		DN1
.....	TACTACTACTACTACGATGGACGTCTGGGGCCAAAGGGAC		DXP'1
.....	GAGGGGGGTTtattactatggttcggggggttatta		DHQ52
.....	GAGGaaactgggaCCAT	
.....G.....	

CDR III

FIG. 66A-2



	20	30	40	50	52 a	53	60
VN251.G1	1CTCTGAAGATCTCTCTGAAGGGTTCTGGATACAGCTTTACCGACTTGGATCGGCTGGGTGCCCGCAGATGCCCGGGAAGGCTGGAGTGGGATCATCTATCTGGTACTCTGTATACGATACAGCCGTCTTCCAAGGCCAGGTC						
J2	CT
3204.sp28
J3
3204.ln10
J4
3204.ln3
3204.ln7
3204.ln8
3204.ln14
3204.ln15
3204.sp22
3204.sp26
3204.sp27
3204.sp30
J5
3204.sp19
J6
3204.sp20

CDR I

CDR II

FIG. 66B-1

70 80 82 a b c 83 90

AACCATCTCAGCCGACAAGTCATCAGCACCGCCCTACTCTGCAGTGGAGCAGCCTGAGGCCCTGGACACCCCATGTATTACTGTCCGAGA
.....
.....
..... T
..... T
..... T
..... G
..... T
..... T
..... T
..... A
..... A
..... A

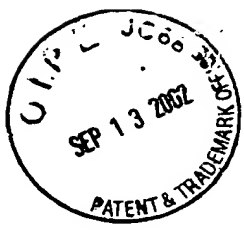
	20	30	40	50	52 a	53	60
VH251.GL	TCTCTGAAGATCTCTCTGAAGGGTTCTGGATACAGCTTTACCACTACTGGATCGGCTGGGTGGCGCAGATGCCCGGAAGGCTGGAGTGGATGGGATCATCTATCTCTGGTGACTCTGTATACCAGATACAGCCCTCTTCC						CAAGGCCAGGTC
2357.m1
2357.m2
2357.m5
2357.m6
2357.m7
2357.m12
2357.m13
2357.m14
2357.m16T.....
2357.m17
2357.m18
2357.m19
2357.m20
2357.m22
2357.m26G.....
2357.m27A.....
2357.m28C.....
2357.m29
2357.m30
2357.m31
2357.m32
2357.m33
2357.m35A.....
2357.m36

CDR I

CDR II

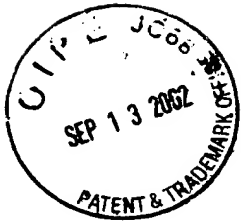
FIG. 67A





20 30 40 50 52 a 53 60
VH251.G1 TCCTGAGATCTCTGTAGGGTTCTGGATACAGCTTTACCAAGCTACTGGATCGGCTGGGTGCCGAGATGCCCGGAAGGCTTGGAGTGGATGGGATCATCTATCTCTGGTGAATCTGTATCCAGATACAGCCCGTCTTCCAGGCCAGGTC
J2C.....G.....
2357.g5
J3
2357.g10
2357.g24
J4T...T..GA.....C.....G.....
2357.g1
2357.g2
2357.g3C.A.....GG.....
2357.g4T...G.....
2357.g6A.....
2357.g11
2357.g17T...T...C.....A.....T.....
2357.g19G.....
2357.g23
2357.g27
2357.g30C..T.....
2357.g32T.....A...T..T.....
2357.g34
2357.g36
J5A.....C.....
2357.g25
2357.g35
J6A...T..C.....A.....
2357.g18
2357.g22C.....T.....C.....
2357.g28G..A.....T.....T.....C.....
2357.g33
COR I
COR II

FIG. 67B-1



70 80 82 a b c 83 90
ACCATCTCAGCCGACCAAGTCCATCAGACCGCTACTCTGAGTGGAGCAGCTCGAGGCTCGGACACCGCCATGTATTACTGTGCGAGA

.....CG.....	CAGGGGGGGGATA	TACTGGTACTTCGATCTCTGGGGCCGTGGCACCTCTGGTC	DHQS2
.....	CATTGcctaAtgaggatGCTTTTGATATCTGGGGCCAGGGGACATGGTC	DXP1
.....GT.T.....	CgggattatcagatatttttgactggtttattatGCG	TACTTTGACTACTGGGGCCAGGGGAACCTCTGGTC	DXP'1
.....A.C...G...T.....	GggattattatgAttcggggactttattataaGCTACCCA.....T.....	DHQS2
.....T.....	ctaactggGCTA.....	
.....T.....	CATCTTA.....	
.....T.....	CAAGGGA.....	
.....T.....	CATCTTA.....	
.....T.....	CAAACTA.....	
.....G.....	CAtggtatagcagctggttagtggttcGACCCA.....	DNL/DW2r
.....T.....	CAGGGCA.....	
.....T.....	CATCTTA.....	
.....G.....	GcgggtatGcagcagctggtTT.....	DW1
.....CG.....	CATCTTA.....	DXP'1
.....	GtgggtcggggatttattatT	
.....	CAAGGGG	
.....G	GGATCGTG	
.....	CTCCCCAATGACAGT	AACTGGTTCGACCCCTGGGGCCAGGGGAACCTCTGGTC	DXP'1
.....G.....	CGGGGctactatggttcggggagttattat	
.....	TACTACTACTACTACGGTATGGAGCTCTGGGGCCAGGGGACACCGTC	DW1
.....	CATGagcagctggtacAGGTT.....	
.....	GATATGGGGGGGCTTCC..C..G.....	
.....C.....	CG	
.....A.....	CG	

CDR III

FIG. 67B-2

[illegible][illegible]

Ggataggttcggggagttatgg
 GAGAGTCTTcaactgggg
 Ggataggttcggggagttatgg
 GGGctacgatattttgactgggtattattGacTCGCT
 GGGctacgatattttgactgggtattattGacTCGCT
 TACTACTACTAC
 GATCAGCGCGGctatagtgggctacggGTCGGGG
 GATCAGCGCGGctatagtgggctacggGTCGGGG
 CctattactatggttcggggagtttatAG
 CctattactatggttcggggagtttatAG
 GAGGgagactacG

 GAGCAGactcggggatCTCGGT
 GAACTATT
 GGCAGctactagg
 ACAGAGTcAGGGatagagatTCGGAC

GACGAGactggggaTCTCGGT
GAACTTATTT
GGCAGctaactgg
ACAGAGTGGGGatagaaaTGG

GAACCTTATT
GGCAGctaact
AGAGAGTGAGG

CDR III

FIG. 68B



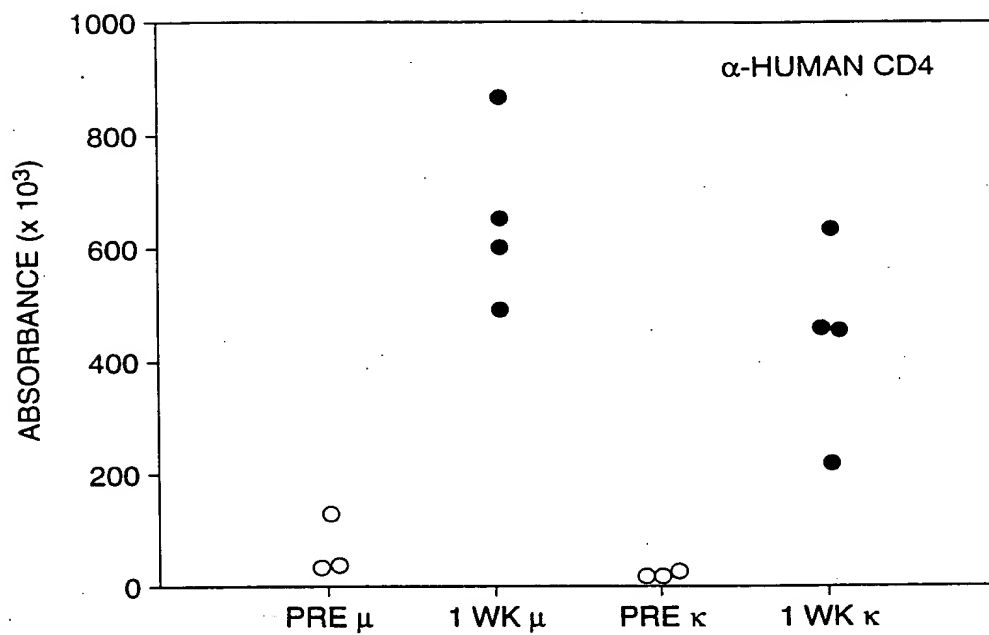


FIG. 71A

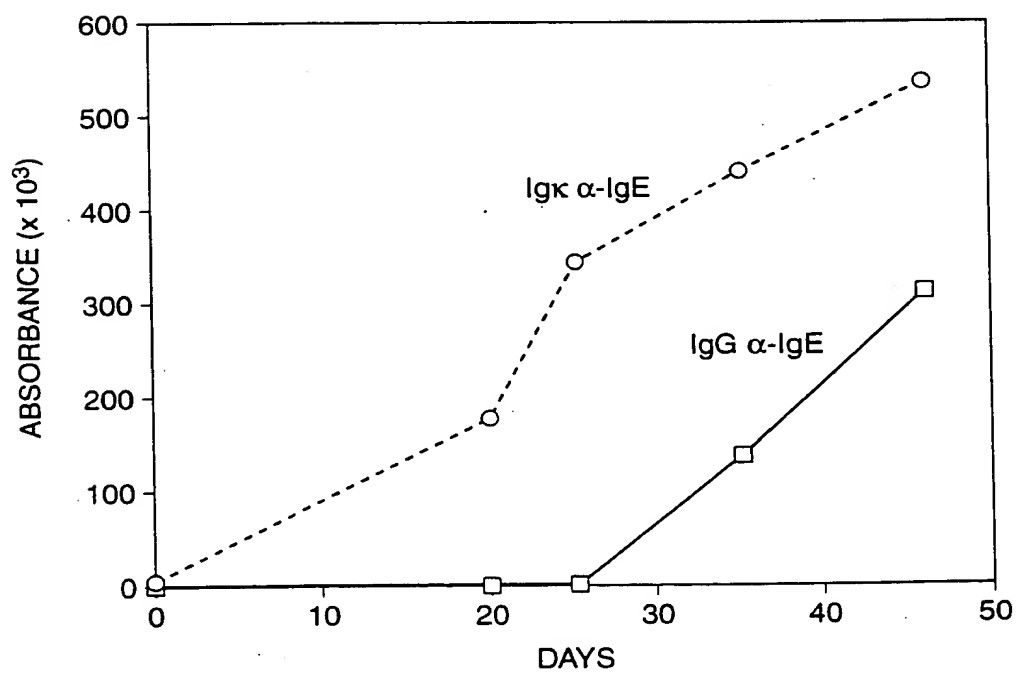


FIG. 71B

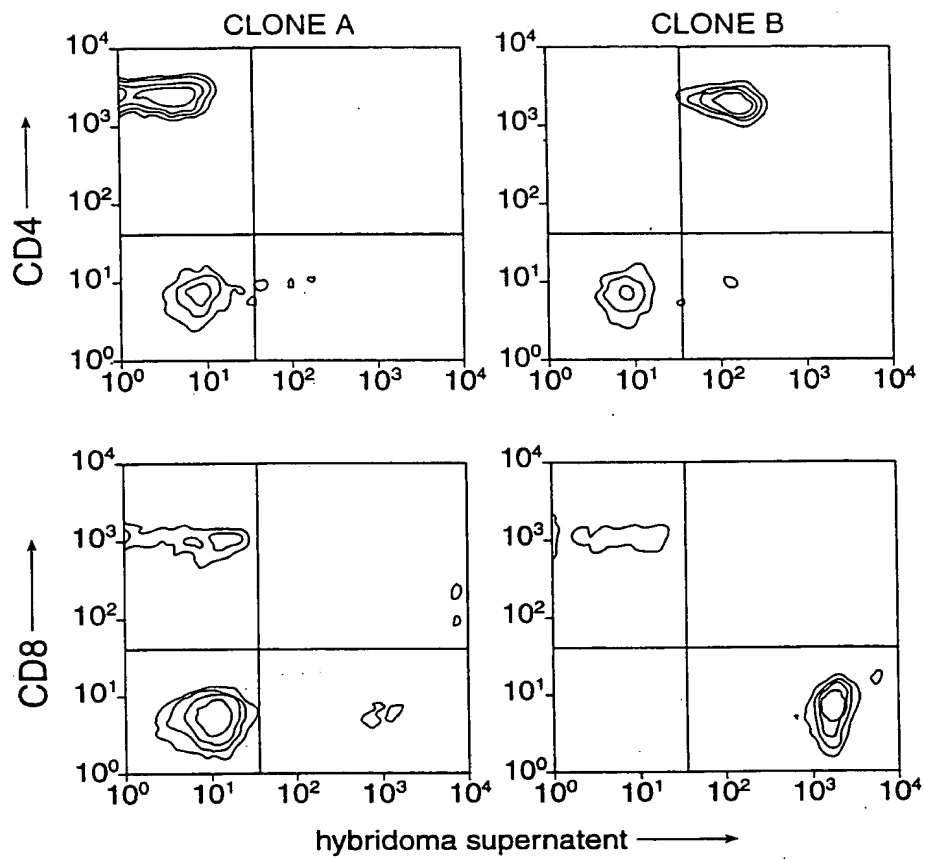


FIG. 72

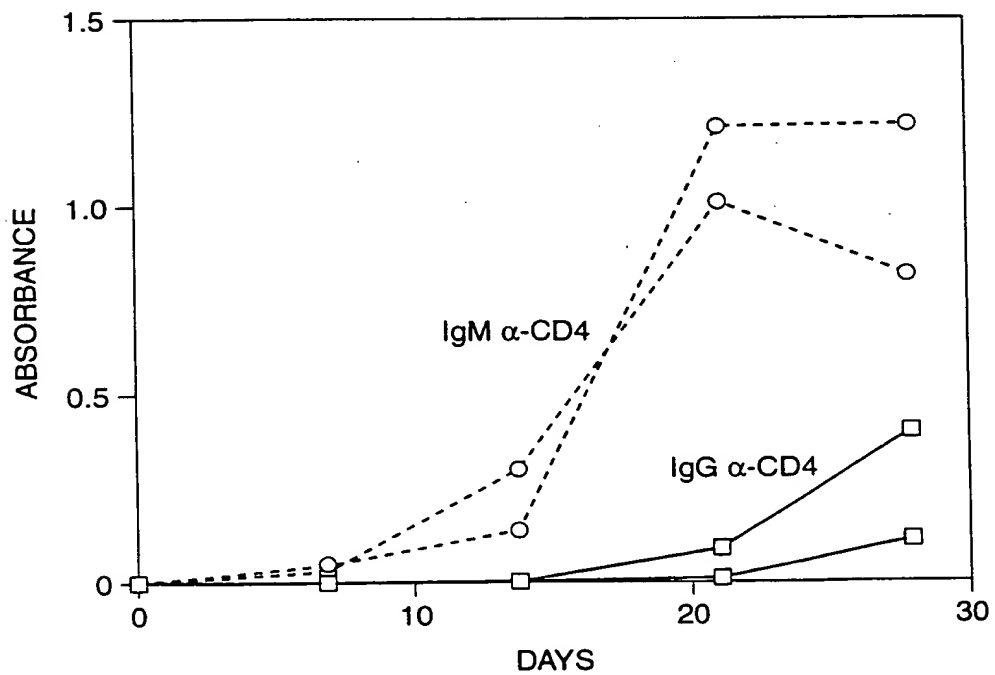


FIG. 73

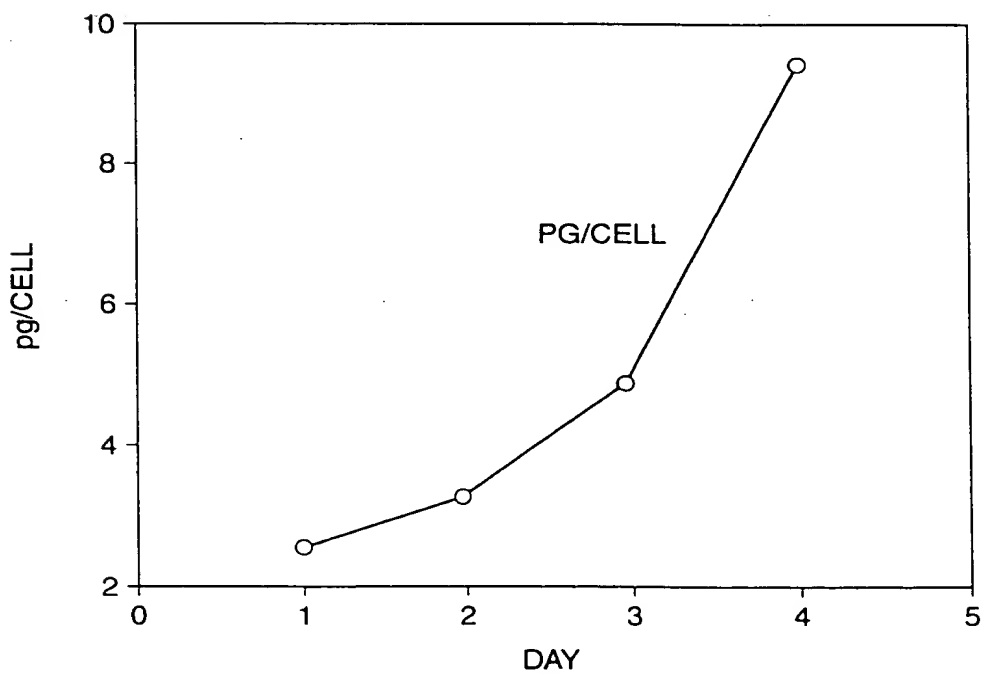
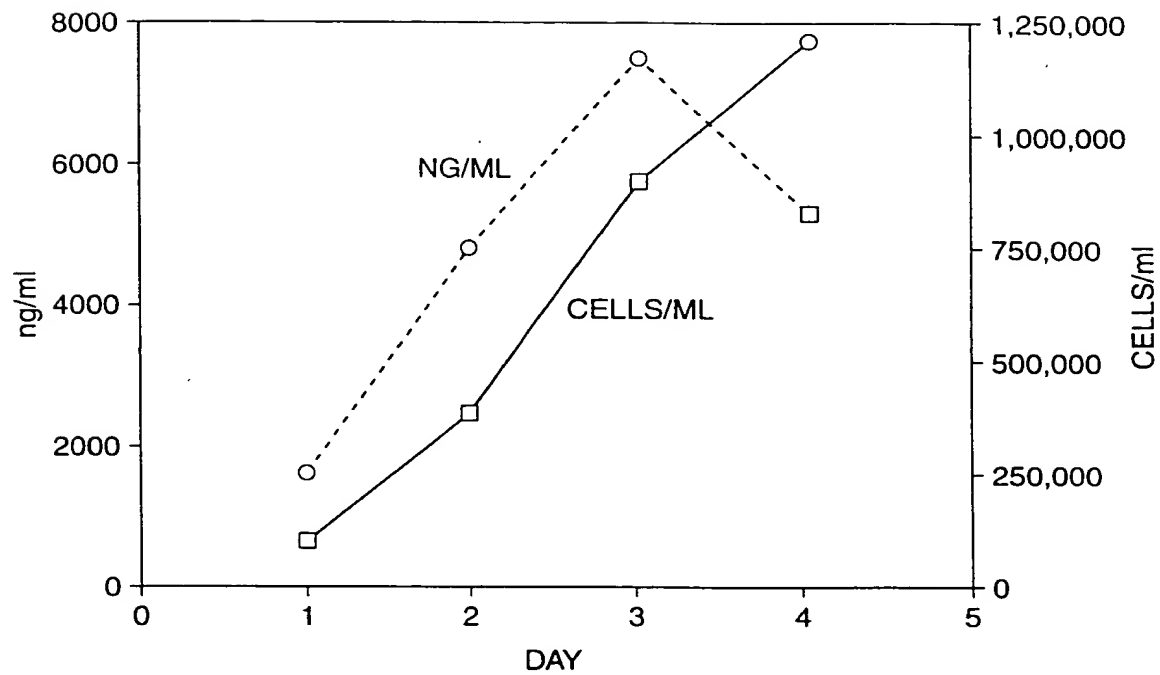
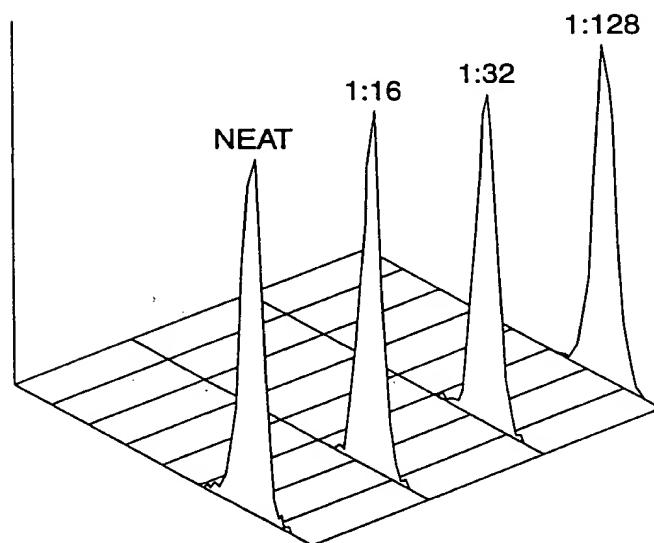


FIG. 74

RPA-T4/2C11-8
#12:BDPHARMCOMP004\FL2-H\FL2-HEIGHT



Leu-3a/2C11-8
#12:BDPHARMCOMP025\FL2-H\FL2-HEIGHT

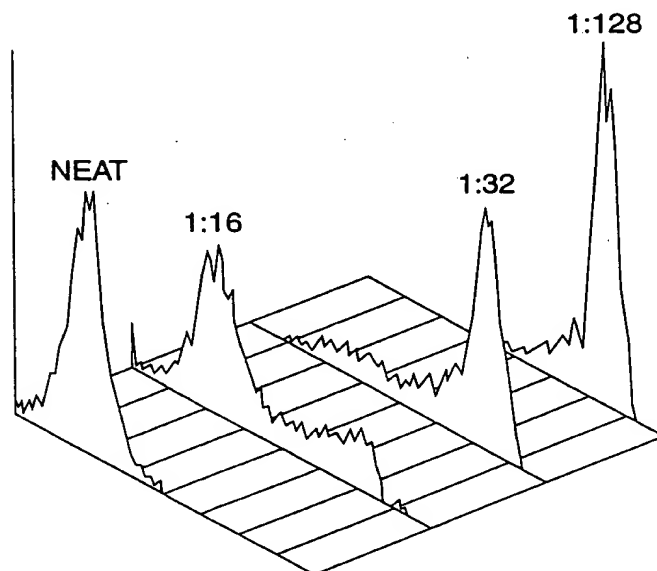


FIG. 75

0 20 40 60 80 100 120 140 160 kb

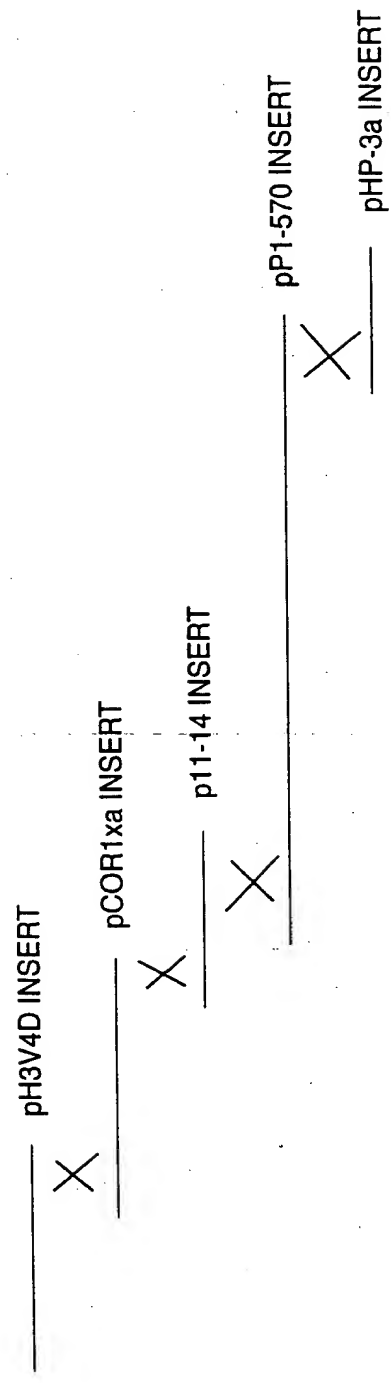


FIG. 76



pGP2b sequence:

AATTAGCggccgctgtcgacaagcttcgaattcagtatcgatgtggtacctggatcctcgagtgcGGCCGCAGTATGCAA
AAAAAAGCCCGCTCATTAGGCGGGCTCTTGGCAGAACATATCCATCGCGTCCGCCATCTCCAGCAGCCGCACGCGGCGCA
TCTCGGGCAGCGTTGGGTCTTGGCCACGGGTGCGCATGATCGTGCTCCTGTCTGTTGAGGACCCGGCTAGGCTGGCGGGGT
TGCCTTACTGGTTAGCAGAATGAATCACCGATACGCGAGCGAACGTGAAGCGACTGCTGCTGCAAAACGTCTGCGACCTG
AGCAACAACATGAATGGTCTTCGGTTTCCGTGTTTCGTAAAGTCTGGAACCGGAAGTCAGCGCCCTGCACCATTATGT
TCCGGATCTGCATCGCAGGATGCTGCTGGCTACCCTGTGGAACACCTACATCTGTATTAACGAAGCGCTGGCATTGACCC
TGAGTGATTTTTCTCTGGTCCCGCCGCATCCATACCGCCAGTTGTTTACCCTCACAACGTTCCAGTAACCGGGCATGTTT
ATCATCAGTAACCCGTATCGTGAGCATCCTCTCTCGTTTCATCGGTATCATTACCCCATGAACAGAAATTCCCCCTTAC
ACGGAGGCATCAAGTGACCAAAACAGGAAAAACCGCCCTTAACATGGCCCGCTTTATCAGAAGCCAGACATTAACGCTTC
TGGAGAAACTCAACGAGCTGGACGCGGATGAACAGGCAGACATCTGTGAATCGCTTCACGACCACGCTGATGAGCTTTAC
CGCAGCTGCCTCGCGCGTTTCGGTGATGACGGTGAAAACCTCTGACACATGCAGTCCCGGAGACGGTCACAGCTTGCT
GTAAGCGGATGCCGGGAGCAGACAAGCCGTCAGGGCGCGTCAGCGGTGTTGGCGGGTGTGCGGGCGCAGCCATGACCC
AGTCACGTAGCGATAGCGGAGTGTATACTGGCTTAACATATGCGGCATCAGAGCAGATTGTACTGAGAGTGCACCATATGC
GGTGTAATAACCGCACAGATGCGTAAGGAGAAAAATACCGCATCAGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTG
CGCTCGGTCGTTCCGGTCGCGGAGCGGTATCAGTCACTCAAAGCGGTAATACGGTTATCCACAGAATCAGGGGATAA
CGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATA
GGCTCCGCCCCCTGACGAGCATCACAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATAC
CAGGCGTTTTCCCCCTGGAAGCTCCCTCGTGCCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCTTTCT
CCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCAGCTGTAGGTATCTCAGTTCCGGTGTAGGTGCTTCCGCTCCAAGCTGG
GCTGTGTGCACGAACCCCCCGTTACGCCGACCGCTGCGCCTTATCCGGTAACATATCGTCTTGAGTCCAACCCGGTAAGA
CACGACTTATCGCCACTGGCAGCAGCCAggcgcgccttggcctaagaggccaCTGGTAACAGGATTAGCAGAGCGAGGTA
TGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTC
TGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAAACAAACCACCGCTGGTAGCGGTGGTTTT
TTTGTTCGCAAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGTCTGACGC
TCAGTGAACGAAACTCAGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATT
AAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCA
CCTATCTCAGCGATCTGTCTATTTTCGTTTCATCCATAGTTGCCTGACTCCCGTCGTGTAGATAACTACGATACGGGAGGG
CTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGCCACGCTACCGGCTCCAGATTTATCAGCAATAAACCCAGC
CAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCCTCCATCCAGTCTATTAATTGTTGCCGGAAGCT
AGAGTAAGTAGTTCCGCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTGCAGGCATCGTGGTGTACGCTCGTCTGTT
TGGTATGGCTTCATTACAGTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCATGTTGTGCAAAAAAGCGGTTA
GCTCCTTCGGTCTCCTCCGATCGTTGTGAGAAGTAAAGTTGGCCGAGTGTATCACTCATGGTTATGGCAGCACTGCATAAT
TCTCTTACTGTATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAAGTCAACCAAGTCATTCTGAGAATAGTGTAT
GCGGCGACCGAGTTGCTCTTGGCCGGGTCAACACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCA
TTGGAAAACGTTCTTGGGGCGGAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCA
CCCAACTGATCTTCAGCATCTTTTACTTTACCCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAA
GGGAATAAGGGCGACCGGAAATGTTGAATACTCATACTCTTCTTTTCAATATTATTGAAGCATTTATCAGGGTTATT
GTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCGGAAAAGTG
CCACCTGACGTCTAAGAAACCATTATTATCATGACATTAACCTATAAAAATAGGCGTATCACGAGGCCCTTTCGTCTTCA
AG

FIG. 77A

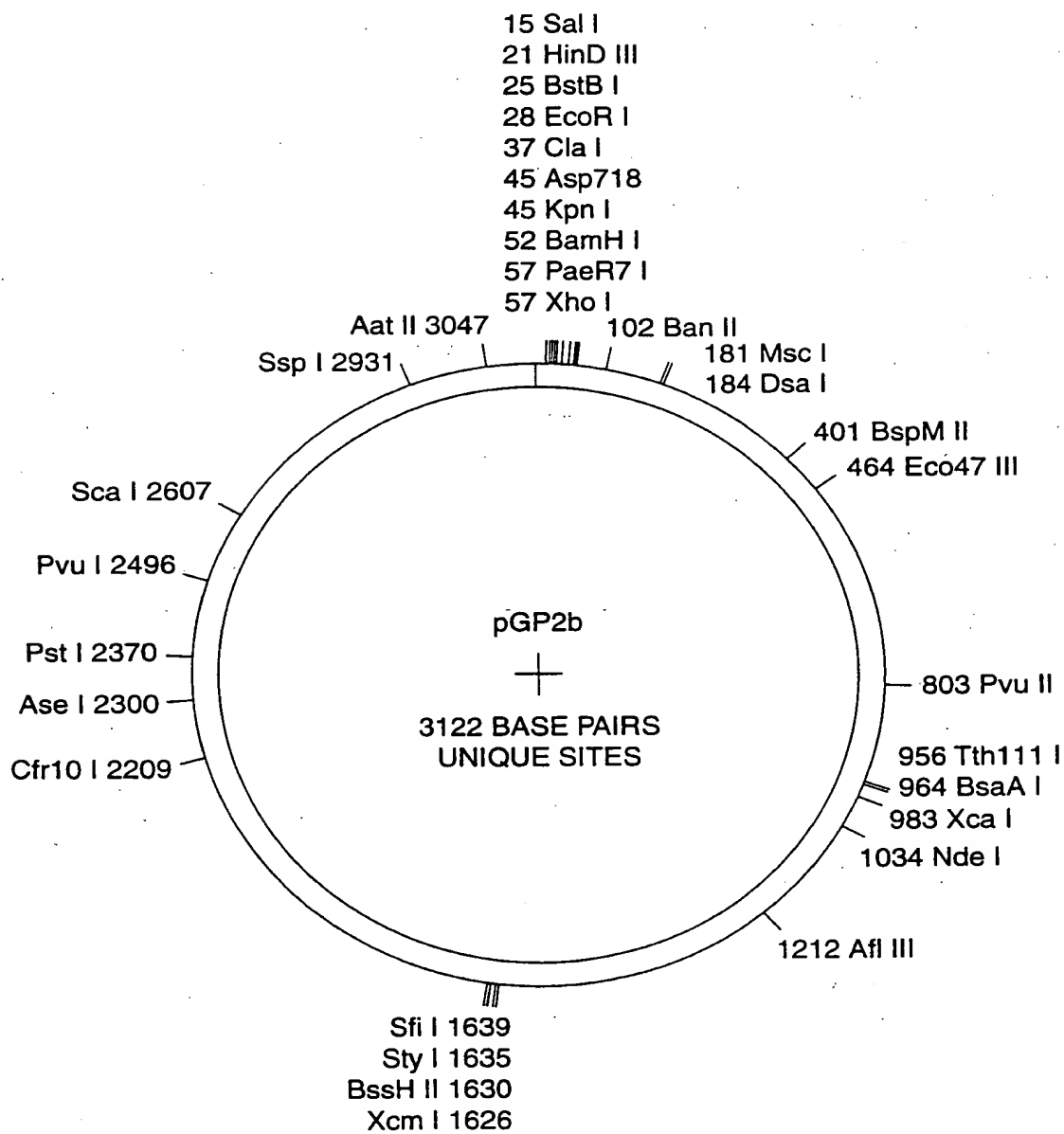


FIG. 77B

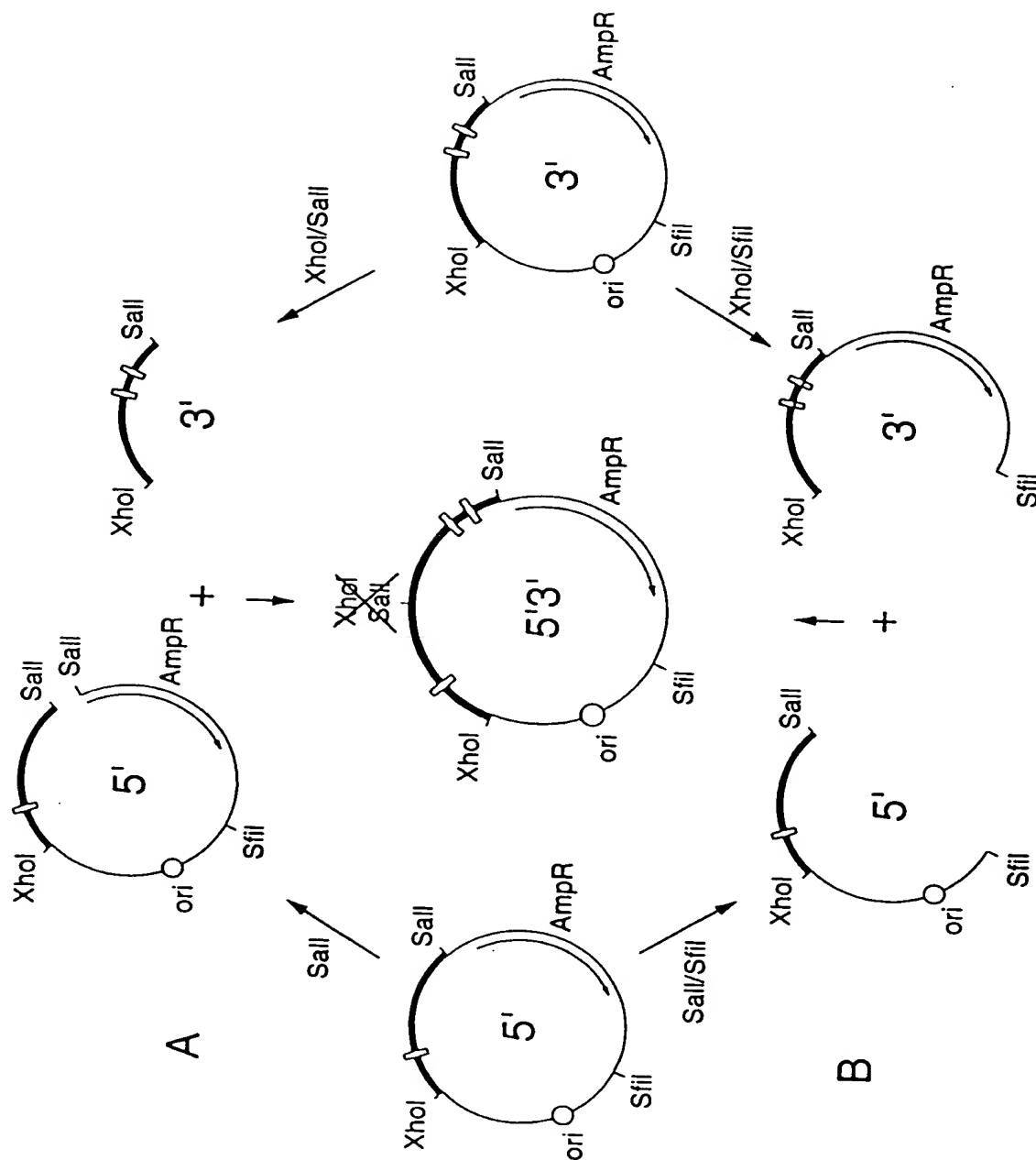


FIG. 78

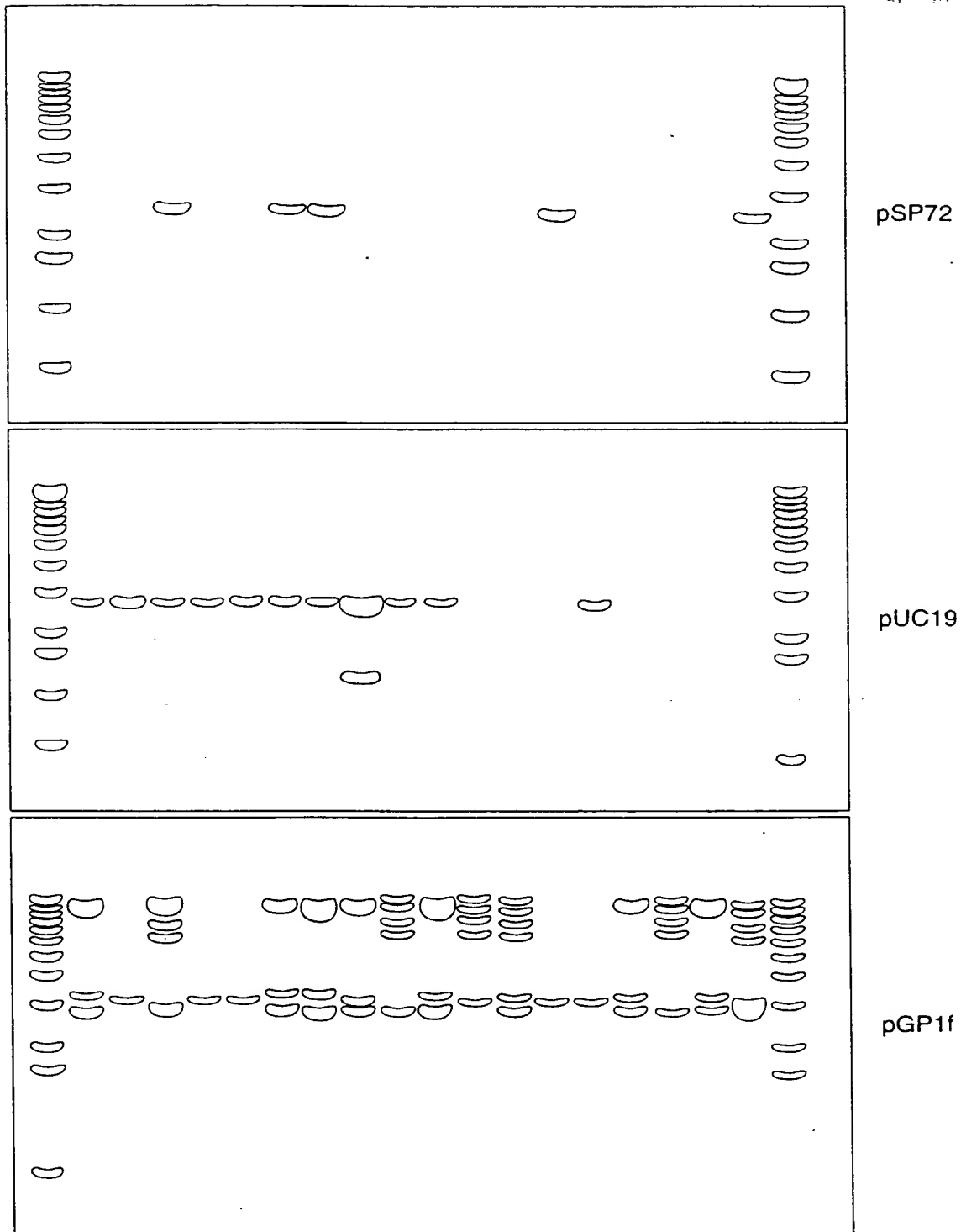


FIG. 79

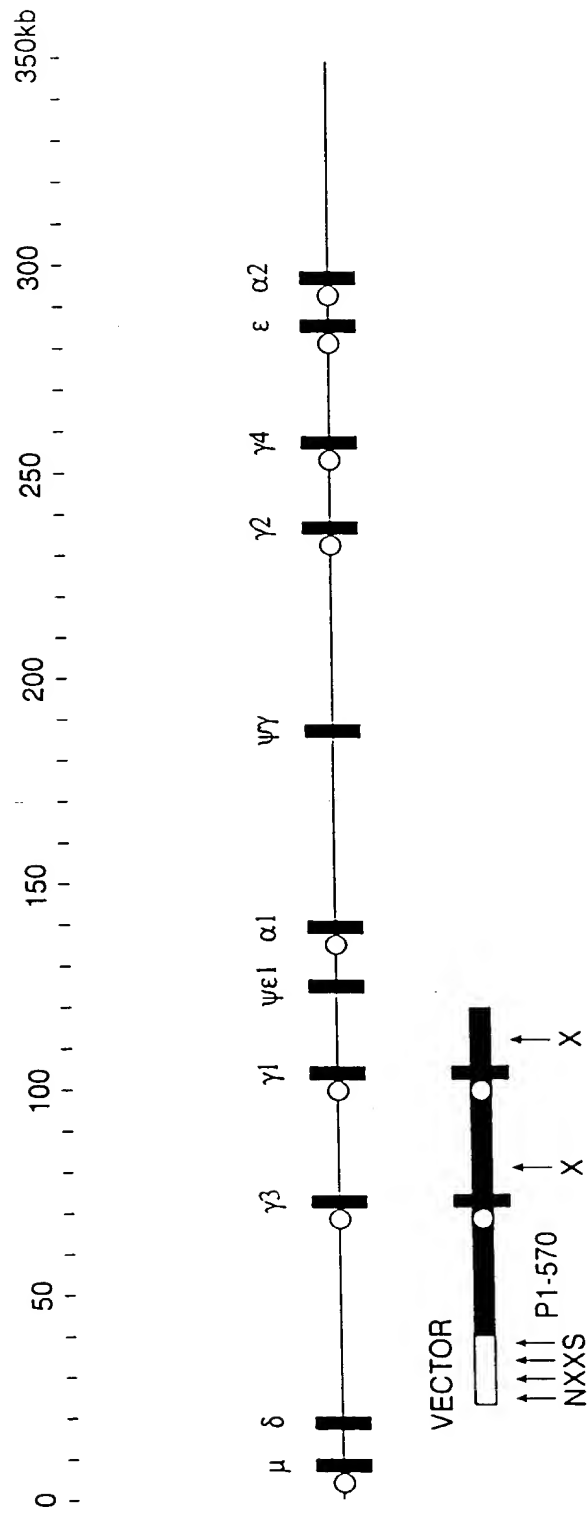


FIG. 80

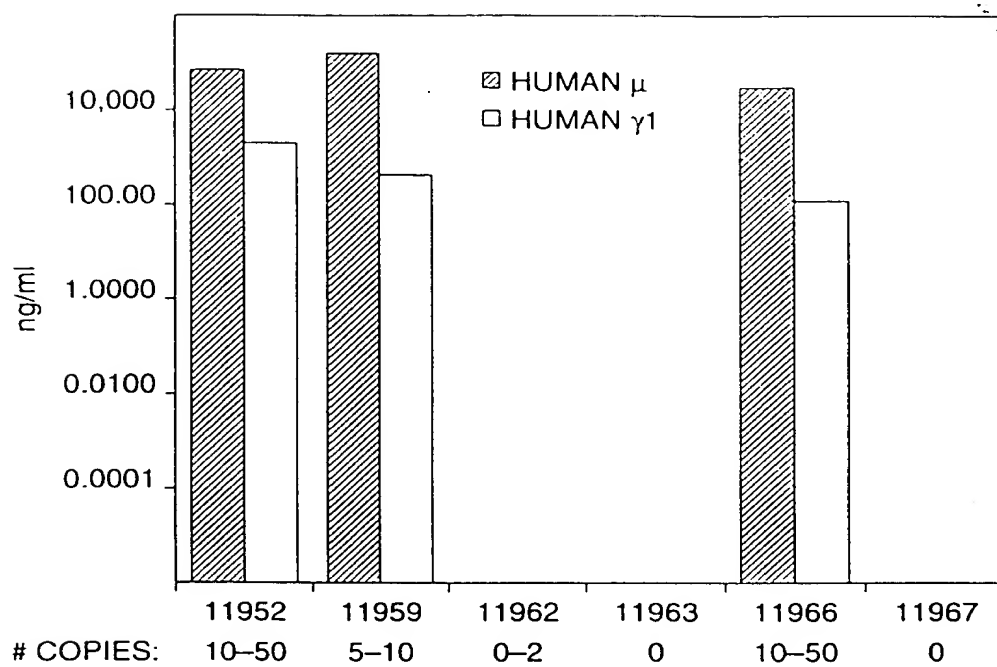


FIG. 81

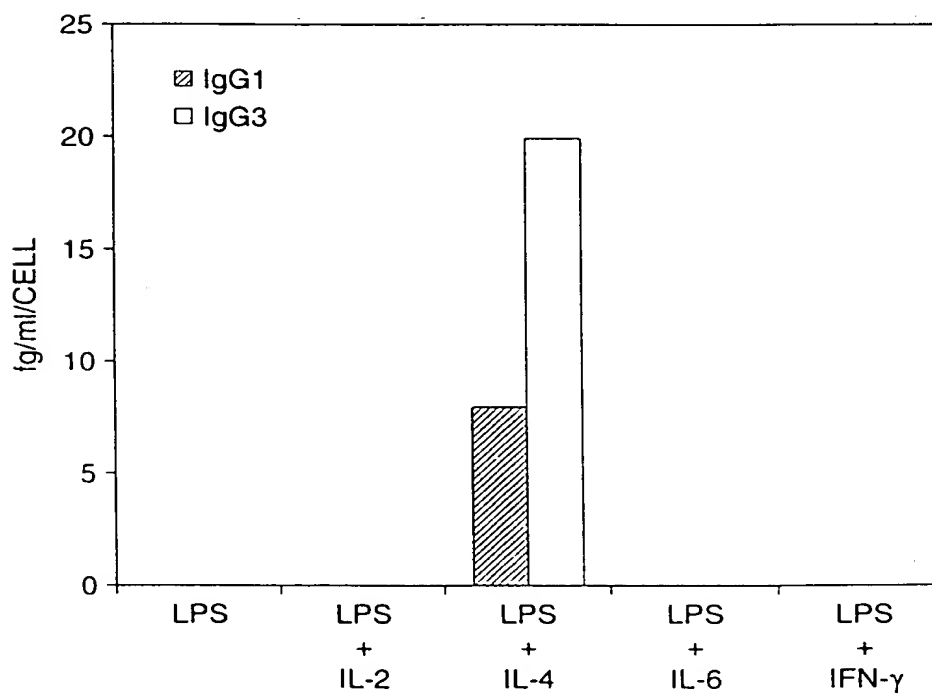


FIG. 84

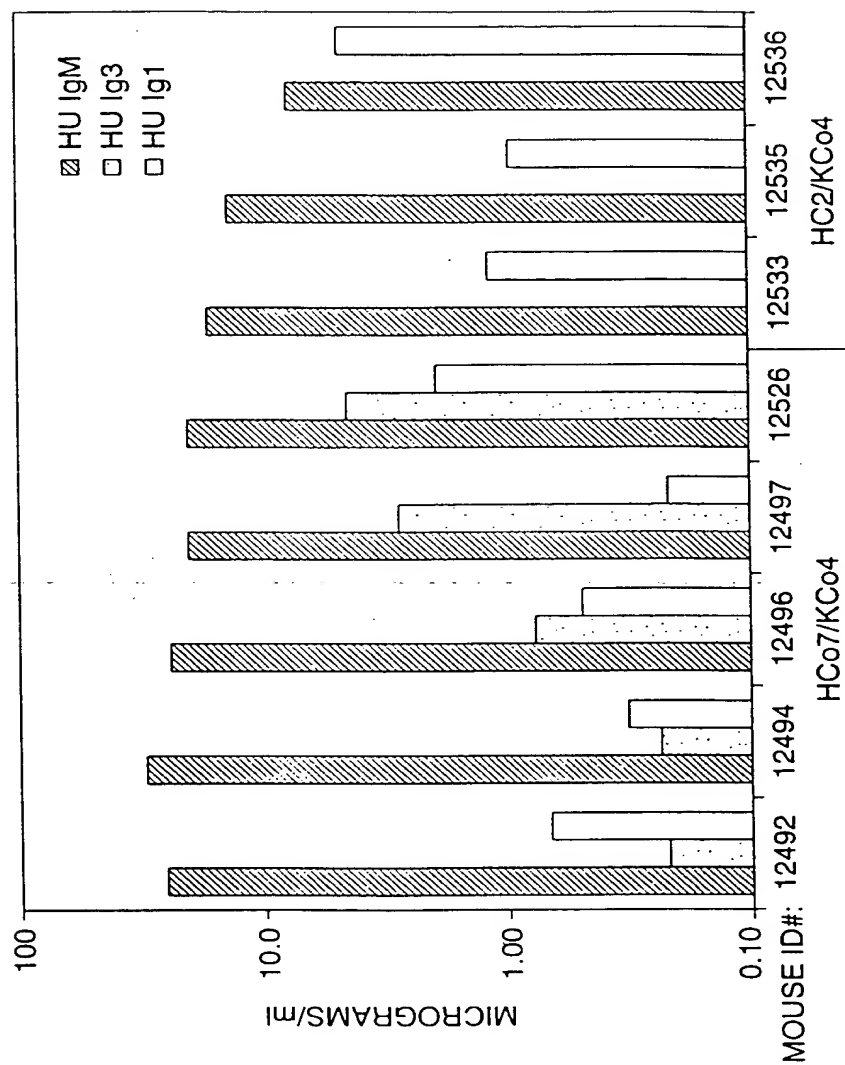


FIG. 82

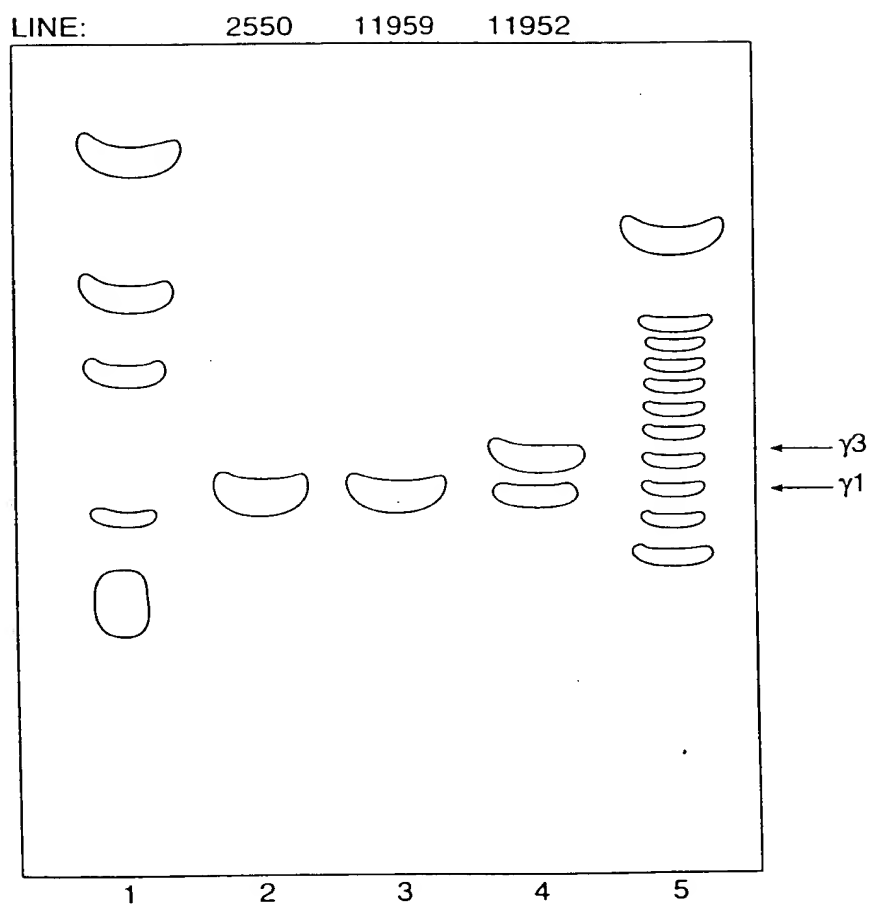


FIG. 83

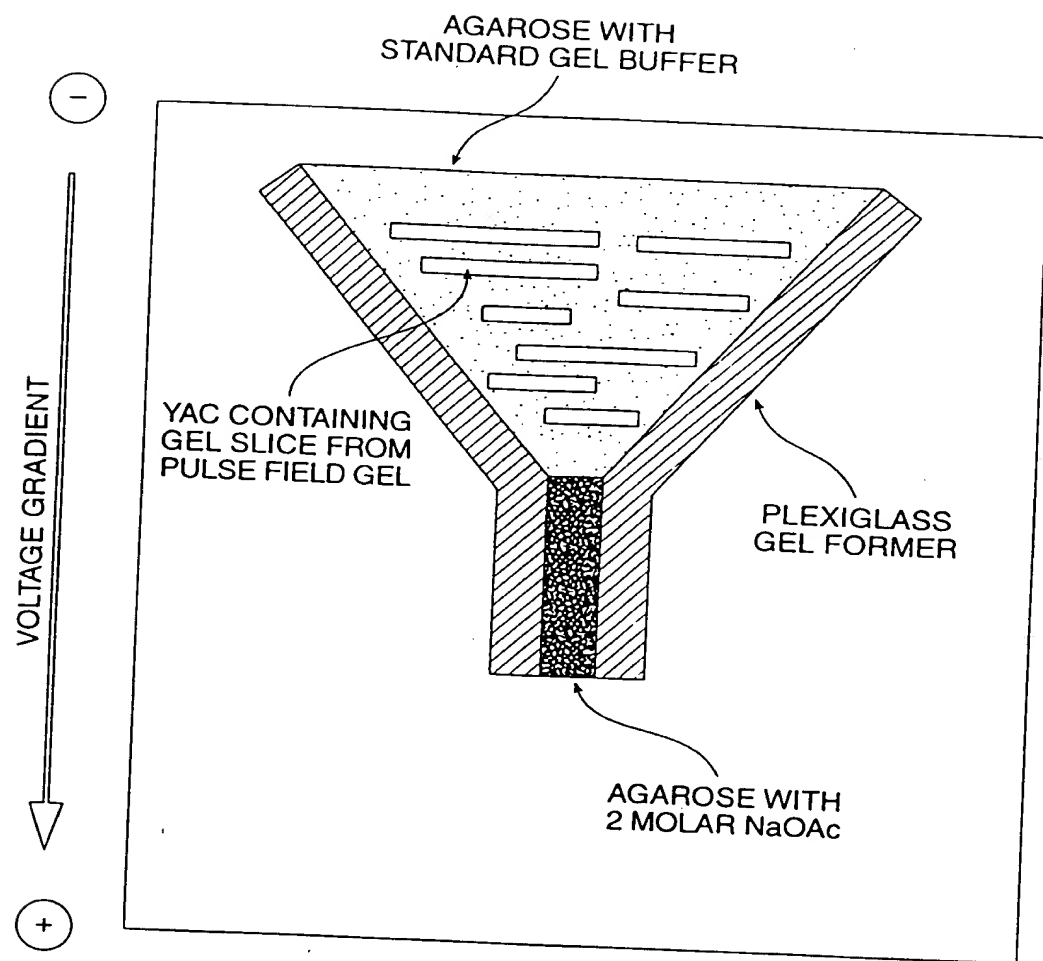


FIG. 85

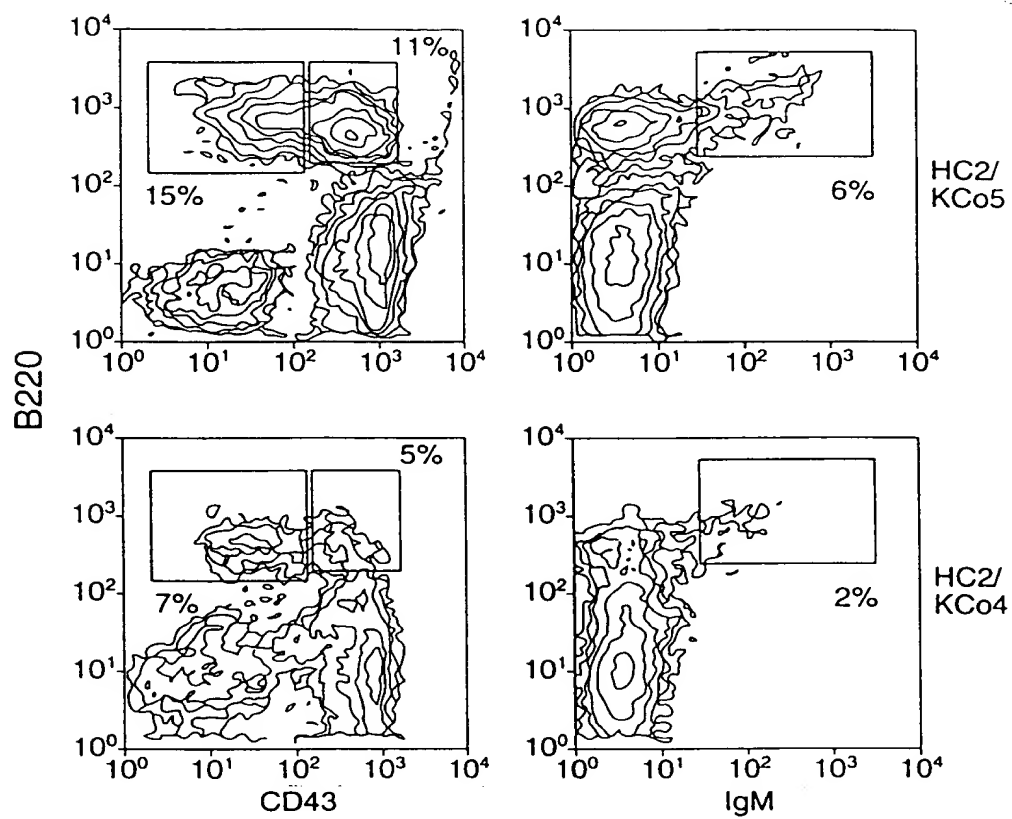


FIG. 86

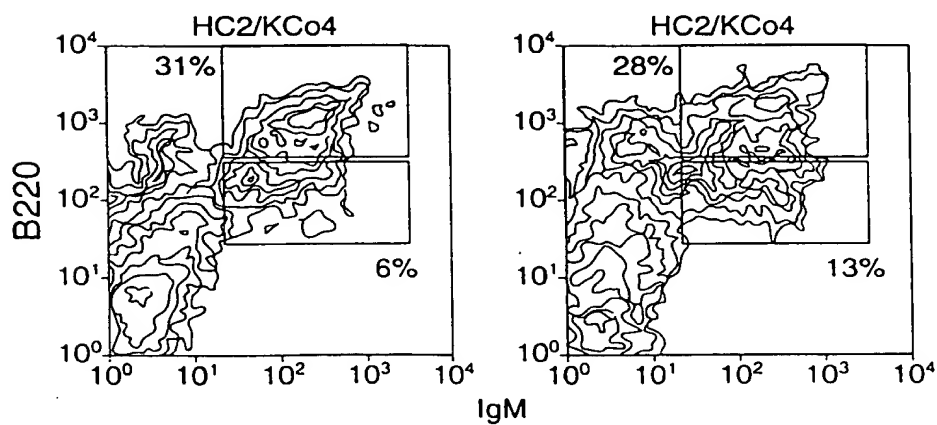


FIG. 87

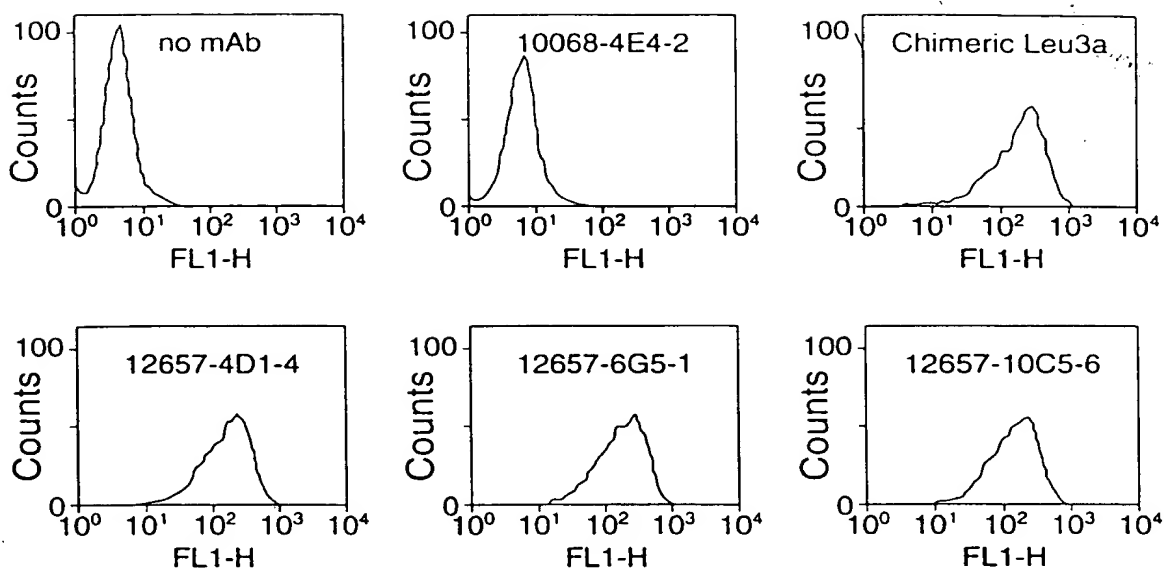


FIG. 88

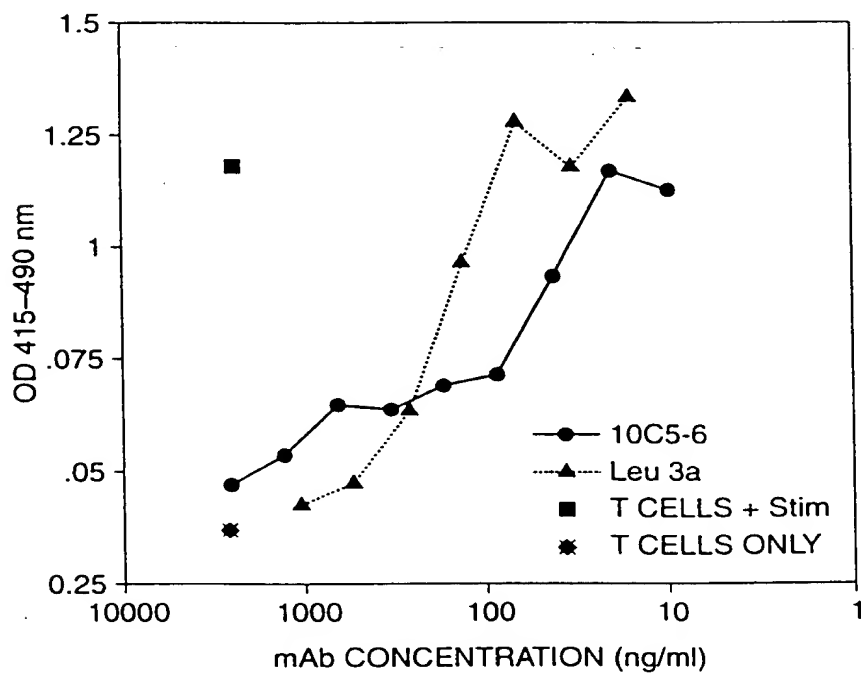


FIG. 90

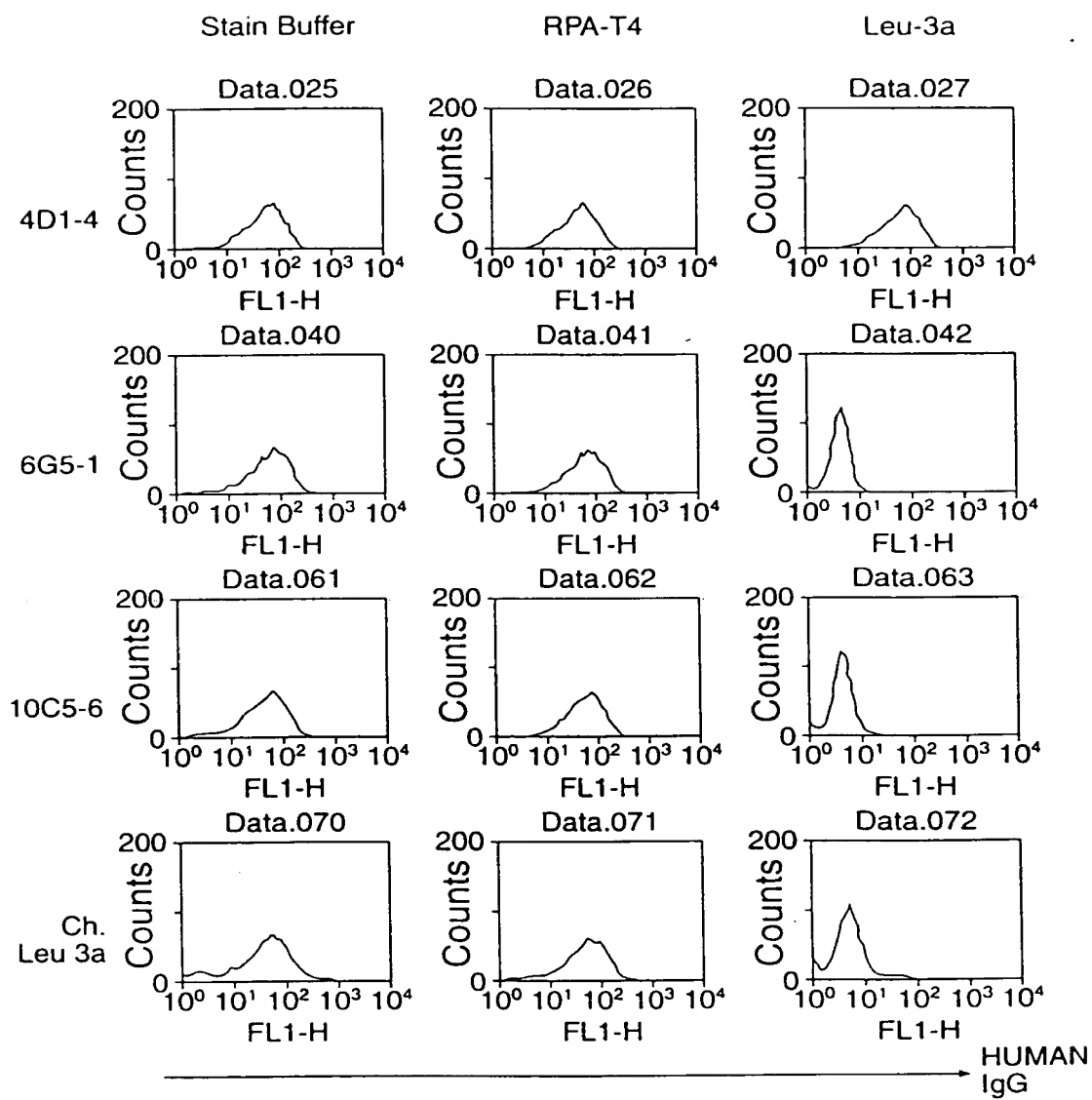


FIG. 89